A South African research agenda to investigate the potential environmental, health and safety risks of nanotechnology

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ABSTRACT

The South African perspective on nanotechnology, recently articulated through its national strategy, envisages nanotechnology to provide solutions to some of the country's key development challenges, such as the provision of safe water and the innovative delivery of health services. The adoption of nanotechnology is therefore being encouraged and nanomaterials are being manufactured on a small scale for research and development purposes. The national strategy places the most emphasis on supporting the design, manufacture, synthesis and characterisation of nanomaterials and developing human capital and infrastructure. However, South Africa has yet to develop a national research strategy to investigate the environmental, health and safety risks of nanotechnology. This paper provides a brief overview of the risk-related research challenges that have been reported internationally. These challenges form the basis of a research framework and a prioritised agenda is proposed to take research forward in the South African context. Ultimately, a greater understanding of the environmental, health and safety risks will help to ensure the long-term sustainability of nanotechnologies.

INTRODUCTION

Nanotechnology refers to the design, manipulation, precision placement, measurement, modelling or fabrication of matter at nanoscale – with at least one dimension measuring 100 nm or less, and how to control the formation of two- and three-dimensional assemblies of molecular-scale building blocks into well-defined nanostructures. The high promise of nanotechnology for improving the quality of life of humankind (e.g. the provision of potable water, medicine delivery and clean energy), coupled with a remarkable reduction in the demand for feedstock materials in industrial processes and the high degree of versatility evidenced by the wide breadth of its applications in diverse industries, have led to the dramatic growth of the global nanotechnology industry, from under 30 companies in the 1960s to over 1500 companies by the early 2000s.[1] In addition, over 800 company-identified products have already been fabricated worldwide and were available in the markets as of October 2008.[2]

In the near future, nanomaterials will constitute a significant market opportunity for many economic sectors. A recent market survey forecast indicates that, by 2014, the industrial sector will be heavily influenced by nanomaterials, especially in the chemicals, electronics and pharmaceuticals sectors, contributing up to 15% of the global manufacturing output and with an estimated worldwide economic value of $2.6 trillion.[3] Therefore, it is not surprising that governments and the private sector have invested millions of dollars in nanotechnology research and development (R&D).[3] In South Africa, the Department of Science and Technology has, to date, invested over R170 million (approximately $20 million) in different aspects of nanotechnology R&D.

The current funding models are directed mainly towards fundamental investigations and the application of nanoscience and nanotechnology and often overlook risk assessment-based research, which is critical for addressing the potential, unintended consequences of nanotechnology. Because the properties of nanomaterials are distinctive from those of their counterpart macroscale chemicals due to their size, shape, surface charge and surface area – among many other physicochemical properties – the present risk assessment tools used for macroscale materials are inadequate to deal with materials having nanoscale dimensions.[4] Equally important, nanotechnology appears to be a Janus-faced technology because the exploitable properties that make nanomaterials novel and potentially useful to society, also cause them to have unanticipated adverse effects on receptor organisms in natural ecosystems.[5] Thus,

> *if their general properties are substantially different from those of bulk materials or larger particles and the particles are in the same size range as viruses that have developed to penetrate into mammalian cells, then there may be reason to expect their toxic effects to differ from those of the bulk materials.*[5]

Even if nanotechnology is perceived to be no more than small mutations, it is recognised, from an industrial ecology perspective,[6] that similarly to most large-scale production the production of nanomaterials requires energy,[7,8] as well as feedstock chemicals,[9] some of which are toxic to humans and other organisms. An overview of nano-manufacturing methods can be found elsewhere[10] and raises the question whether or not the benefits of using nanotechnology as an alternative to existing technologies really outweigh the impacts of producing nanomaterials, with reference to energy requirements, environmental impacts and disposal-related costs and risks.[11,12,13,14]

Consequently, it is imperative that nanotechnology risks are investigated carefully in relation to environmental, health and safety-related (EHS) aspects, because these are equally important aspects for promoting the long-term sustainability of this new technology.[15,16,17,18] This paper aims to map out a research agenda that may provide a basis for systematic risk assessment research, human capital development, and the establishment of science research infrastructure to support EHS risk research related to nanotechnology in South Africa.

Four features make it essential to set an agenda for assessing the risk of nanotechnology in South Africa. Firstly, the agenda would clarify the best options to achieve a balanced and rational prioritisation of

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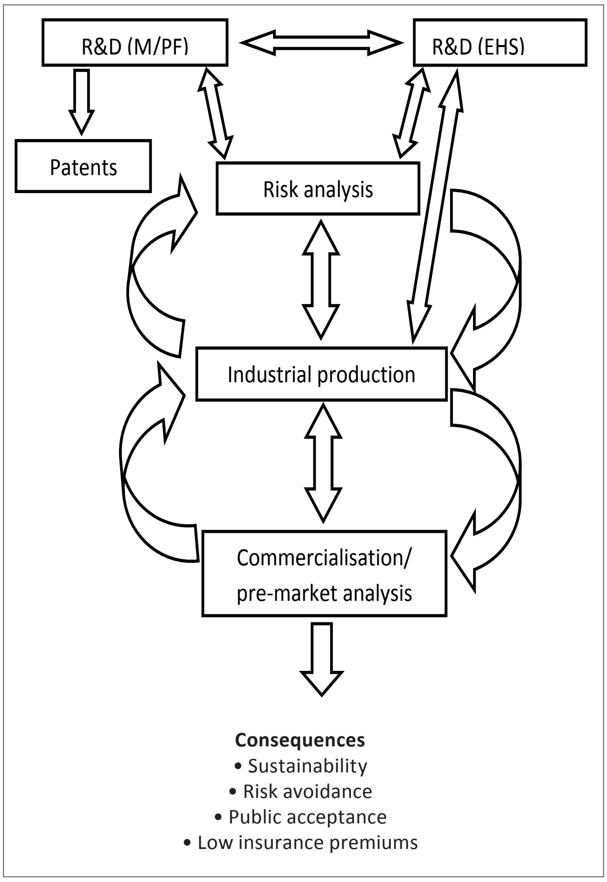
the available funding in the field of nanotechnology. The current funding model assumes that there are no potentially adverse effects associated with nanotechnology. However, the early detection and understanding of risks helps to ensure the long-term effective management of the technology. Previous failures to investigate and manage the risks of various technologies have resulted in devastating effects on humans and ecological systems and, in certain cases, have led to the total ban of these technologies despite their original, intended societal benefits.[19] Secondly, the current levels of pollution arising from industrial and commercial activities in South Africa appear to have reached crisis proportions.[20,21] Therefore, the ability to profile nanotechnology risks at an early stage would avoid adding yet another source of unknown risks, which in turn could exacerbate existing pollution problems. Thirdly, because South Africa is a developing country, it is essential that every individual is protected, together with the ecological systems they depend on, from potential nano-pollution effects. Lastly, but very importantly, an early understanding of nanotechnology risks can assist efforts to re-engineer the fabrication processes in order to reduce the likelihood of any unintended adverse consequences.

RESEARCH CHALLENGES RELATING TO NANOTECHNOLOGY RISKS

Recent scientific literature has highlighted issues pertaining to risk assessment and the difficulties experienced in monitoring and managing nanomaterials.[18,22] This is because numerous types of nanomaterials are currently being fabricated industrially and within R&D environments; these are classified broadly as carbon-based materials, metal oxides, metals, quantum dots or mixtures of different phases. Such materials pose a major challenge to the effective categorisation and prioritisation of ecotoxicological risk assessment[9,22,23] and highlight the need for comprehensive product life cycle analyses – particularly at those points in the product life cycle where these materials may enter into the environment.[23] From systems engineering principles, it is well known that the greatest opportunity to adequately manage a new technology occurs in the design and development phases.[24] Therefore, robust methodologies and protocols need to be developed to assess the potential impacts of nanotechnology during the entire life cycle of a given product or material.



M/PF, manufacturing/particles fabrication.
EHS, environment, health and safety.

FIGURE 1
Proposed cyclic proactive risk-assessment model to address emerging environment-, health- and safety-related aspects of nanotechnology-based materials and products

In this paper, we propose a proactive and adaptive management approach (Figure 1) that can support dynamic monitoring of both the local and systemic potential impacts of rapidly emerging nanotechnology-based products. The proposed approach has several merits when compared to the conventional risk assessment approaches that are currently used (Figure 2). The latter model places emphasis on establishing the impacts of a given technology after it has been on the market long enough for its risks to be quantified. Examples of where these approaches have yielded disastrous effects for different technologies have recently been documented[19]; the lessons learned should provide a sound basis to avoid similar pitfalls with nanotechnologies.[25] Consequently, the adoption of a proactive and adaptive approach would help to safeguard society from being locked into systems that are difficult to reverse.[9]

Other challenges that are presented by nanotechnology highlight the need for risk identification in the early phases of the product life cycle.[26] In our view, this should commence with formal risk assessment, monitoring and management. Specific challenges that nanotechnology has posed to the current risk assessment protocols[9] are briefly summarised in the following subsections.

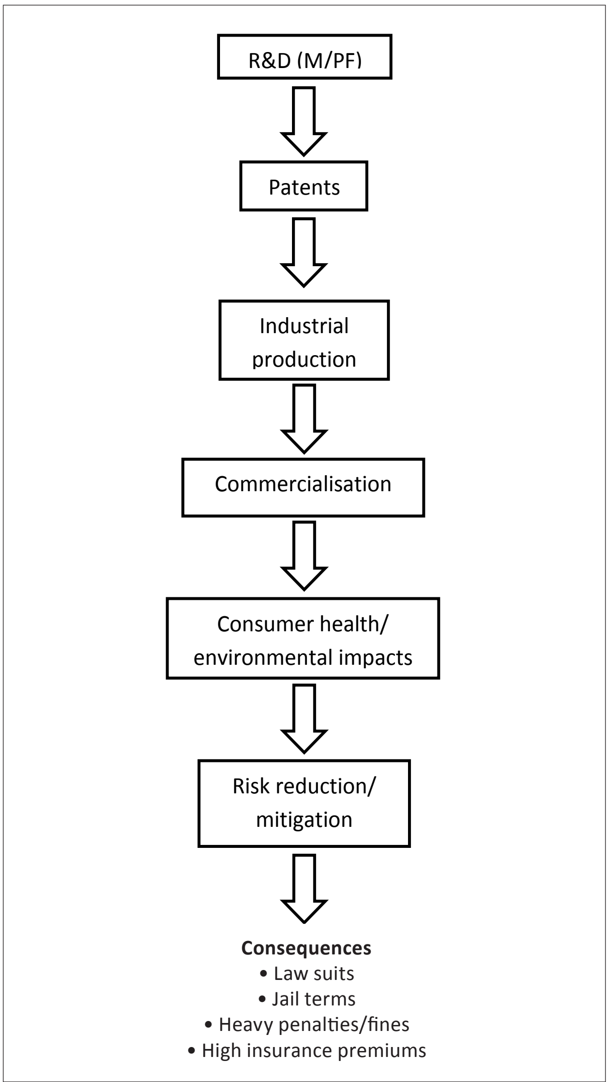
Scarcity of EHS information on nanomaterials

Environment, health, and safety information on nanomaterials is scarce. Nanomaterials may be potentially hazardous due to reactions at a cellular level, especially because of their apparent similarity in size, shape and chemical form to known hazardous materials, such as asbestos and polychlorinated biphenyls. This concern is further exacerbated by a scarcity of toxicological data, which are essential for studies using standardised protocols (e.g. biological system to be studied) with technologically relevant nanomaterials (e.g. uniform nanomaterials in their product form with the necessary coatings and isolated from catalysts used in their synthesis) within their likely exposure pathways (e.g. ingestion of water-entrained nanoparticles). As a result, the development, testing and approval of a routine, formal risk assessment protocol for nanomaterials may take 5–10 years.[16] Therefore, there is a need to develop a metrology that can aid the detection, analysis and quantification of potential risks of nanomaterials in a confined or laboratory environment and extrapolate this to real-world environmental conditions.

Absence of a single index to measure the toxicity of nanomaterials

There is no single index to measure the toxicity of nanomaterials. Presently, toxicity is still being measured and expressed in units of mass per unit volume. The difficulty in interpreting such toxicological data further complicates our ability to discriminate between toxicity owing to macroscale chemicals and that due to the nanoscale properties of a given nanomaterial.[27,28,29,30] Traditionally, dose-response curves have served as a single index for expressing toxicity for most macroscale chemicals. However, for nanomaterials, the response may not always increase predictably as a function of dose because nanomaterial chemical toxicity is not determined by a single factor, such as particle size.

Other physicochemical properties, such as surface charge, shape, degree of aggregation, structure, surface area and the stability of any surface coatings, degree of reactivity, sites and rates of uptake and transport, pH, the presence or absence of organic matter, and zeta potential could be responsible; these factors cause different responses over different dose ranges.[30,31]



M/PF, manufacturing/particles fabrication.

FIGURE 2
Conventional model for risk assessment of products and materials

Early risk identification will help the formulation of potentially useful indices for characterising the toxicity of nanomaterials.

Lack of universal nanotechnology nomenclature

Nanotechnology nomenclature is still under development and, so far, there appears to be little shared understanding. Indeed, the most salient physicochemical characteristics that define a particular nanomaterial are yet to be agreed on universally, and these properties have not yet been linked to the observed toxicity of the nanomaterial. Nanotechnology comprises nanomaterial components spanning several different classes, namely organic, inorganic, ceramic, and even biological in some cases. This makes the classification of nanomaterials exceedingly difficult,[13,32,33] especially within existing regulatory frameworks, thereby confounding regulators.[12,33,34]

Environmental transportation of nanomaterials

The ready environmental transportation of nanomaterials increases chances of exposure. Nanomaterials can easily be distributed throughout an ecosystem due to their small size and solubility and, hence, they can present an increased risk of exposure.[35,36] Even in cases where nanomaterials may be aggregated, they still present a problem.[37] The higher mobility of nanomaterials in the environment implies a greater potential for exposure to diverse receptor species as they become dispersed over greater distances and their effective persistence in the environment increases.[38]

Absence of cost-effective monitoring systems for nanomaterials

Nanomaterials are not easily monitored in real time and therefore cheap and easy-to-use monitoring technology is not yet in place.[16] For instance, technologies such as electron microscopy require extensive sample preparation, whereas spectrometric methods do not give sufficient 3D information at the nanoscale. It is critical to be able to monitor, characterise and measure nanomaterials to understand human and environmental exposure to nanomaterials, as these abilities will have important implications for occupational health. At present, technologies for these purposes are not readily available[16,31] and are only expected to become available in the market within five to seven years.[16]

Systemic human health and environmental risks of nanomaterials

Nanomaterials may pose system-level human health and environmental risks, where attention to one set or system overlooks the greater impacts.[39] Consequently, the societal effects of nanotechnology are not localised to one community or industry. Instead, nanomaterials that have been applied in one particular environment can easily be transmitted to other environments where there may be insufficient risk data and research. For instance, silver nanoparticles in air fresheners have antibacterial properties. They are intended for use indoors and it is easy to envision human inhalation. However, there are no data on their effects on the digestive or respiratory system in humans.

Similarly, silver nanoparticles used in socks for antibacterial purposes have been shown to result in unexpected increases in the concentrations of biosolids in wastewater systems and are suspected to kill many of the microorganisms that are essential for the optimal functioning of biological wastewater treatment systems.[40] Thus, risks from such system-level impacts on human health span the entire range, from organ systems and others to beyond the point where nanomaterials are applied; this wide range of risks is worrisome in view of the increased quantities of nanostructures likely to occur in the near future. Similar system-level impacts are also possible across different environmental phases.

THE WAY FORWARD

South Africa envisages the exploitation of the benefits of its nanotechnology capabilities, as explained in the *National nanotechnology strategy*[41]. This strategy will be implemented through the establishment of R&D hubs, for example the Council for Scientific and Industrial Research (CSIR).[42] At present, however, South African R&D efforts are directed primarily towards the development of nanomaterials and devices based on nanosciences and nanotechnology principles for application purposes[43]; the risk assessment of nanotechnology has not yet been established in the country. Increasingly, concerns are being expressed both nationally and globally, advocating caution and forethought about EHS issues related to nanotechnology, because these issues have yet to receive the attention they deserve.[17,23] Elsewhere internationally, the precautionary approach is advocated by diverse stakeholders, comprising environmental advocacy groups, multiple government agencies, standards organisations, scientific, as well as engineering and health-related professional societies, academics, trade associations and both large and small industries.[44,45,46,47,48,49,50]

Therefore, we propose several practical strategies that can help to establish a nationally coordinated research programme to investigate the potential adverse effects of nanotechnology. These strategies are broadly grouped into three categories, and each is summarised and discussed in the following sections.

Human capital development

Human capital development is a central concern in terms of producing a new generation of scientists and researchers that are suitably qualified to ensure safe and responsible development of a nanotechnology-based industry in South Africa. Two practical steps for developing such a skilled workforce in South Africa are, (1) a curriculum-based training approach that includes incentive funding and (2) the setting up of research chairs at selected universities and of an advisory forum to assist government decision makers.

Under the curriculum-based approach, the intervention mechanisms proposed comprise:

- The development of sustainable funding mechanisms to support educational programmes at honours, masters, doctoral and postdoctoral levels. Such funding would be essential in developing and offering interdisciplinary and inter-institutional postgraduate programmes in EHS nanotechnology-related research and training. For example, such funding could provide opportunities for promoting collaborative research and educational programmes across different disciplines that contribute to enhancing our collective understanding of the EHS aspects of nanotechnology (e.g. providing support for research teams with diverse expertise).
- The development of stakeholder-specific educational programmes (e.g. for government officials, industry workforce and unions) specifically to provide general information and create the levels of awareness that are essential for promoting familiarisation with issues and risks related to the EHS aspects of nanotechnology.
- The development of training and research programmes to encourage and attract an existing workforce in diverse disciplines to pursue EHS nanotechnology-related career opportunities. Because it will take time to train a workforce from scratch, the current scientific workforce should be encouraged to consider nanotechnology-related careers as well.

On the other hand, the establishment of research chairs and an advisory forum should be tasked with directing and conducting research for the EHS aspects of nanotechnology. In addition, the advisory forum, that should include the research chairs, would provide advice to the national government on policy issues related to nanotechnology risks. The chairs should be funded using a similar model to the current chairs supported by the Department of Science and Technology under the auspices of the South African Research Chairs Initiative.

At present, conventional industries manufacturing macro-scale chemicals and materials are characterised by dedicated departments (e.g. certain government agencies such as the South African Bureau of Standards), with personnel responsible specifically for the management of EHS aspects arising not just from production, but all the way through until the disposal stage of various waste streams. The human capital development model proposed here is envisaged to yield the necessary manpower to play similar roles in nanotechnology-related industries.

Development of state-of-the-art research infrastructure

State-of-the-art R&D infrastructure is essential to the success of a properly functioning national research platform that fosters advanced research in EHS fields relating to nanotechnology. Implicitly, the research infrastructure should enable researchers to study the toxicity and ecotoxicity of a diverse range of nanometre-scale materials. Conversely, some of the equipment currently used in EHS studies for conventional chemicals can also be utilised to investigate the properties of materials at nanoscale, where appropriate.

Such an undertaking has a twofold benefit. Firstly, it allows maximisation of the use of presently available infrastructure and opens potential avenues of collaboration between

TABLE 1
Proposed focused research areas to aid in the assessment of risks posed by nanomaterials to humans and the environment

1. Hazard identification
Particle characteristics
Aspect ratio
Diameter (particle/aggregate)
Surface area/properties
Water solubility
Chemical composition
Emission
Production volume
Material flows
Potential particle releases (production, use, disposal)
Health effects
Humans
Experimental animals
Environmental effects
Persistence
Bioaccumulation
Ecotoxicity
Long-range transport
Environmental factors (pH, humic acid, zeta potential, etc.)
Biomagnification
Mechanisms of nanomaterials trophic transfers
Nanomaterials influence on bioavailability and toxicity of other environmental pollutants
2. Hazard characterisation
Epidemiological studies
Workers
Customers
Exposed population
In vivo studies
Acute/chronic toxicity
Aquatic systems
Other different species
In vitro studies
Human/animal, different cell types
Models (lung, skin, systemic effects, gut, etc.)
Computational toxicology
3. Exposure assessment
Exposure routes
Inhalation, dermal, injection, oral
Classifications
Nanomaterials
Generated nanowaste streams
Environmental monitoring
Life cycle assessment
Environmental uptake
Occupational monitoring
Personal exposure
4. Risk assessment
Susceptibility extrapolation models
High dose → low dose
Animal → human
Human → wildlife
Prediction models
QSARs type models specific to nanomaterials
Threshold value calculation
Intake, emissions concentration, max workplace concentration

(Table 1 continues on the next page.)

TABLE 1 (Continues...)
Proposed focused research areas to aid in the assessment of risks posed by nanomaterials to humans and the environment

5. Risk management
Preventive measures
Personal protection equipment
Modification of processes
Operational procedures
Standardisation
Measurement techniques
Toxicological assessment
Ecotoxicity assessment
Regulation
Exposure/emission standards
Production standards/restrictions
Waste/by-products management protocols

institutions through the sharing of equipment. It also ensures that scarce funding is not utilised unnecessarily to duplicate the available equipment. Secondly, such an approach will allow the clear identification of those specialised and advanced items of equipment that can be classified as multi-user national facilities, which can then be housed in central locations that are accessible to researchers from all interested stakeholder groups, such as academia, industry, government departments and environmental law enforcement agencies.

The proposed centralised infrastructure is envisaged to support a range of research activities, and to provide the capability to analyse diverse materials, as well as test different organisms for toxicity. The key functions of the centralised infrastructure should include:

- The development of measures to raise awareness among the nanotechnology EHS research community of the services that are available in the national network of facilities, and of the possible opportunities for collaboration with other national and international researchers.
- Periodic upgrading of the facilities to ensure that the facilities and equipment remain state-of-the-art and are able to cope with newly-emerging nanomaterials.
- The provision of expert advice, expertise and collaboration and, where necessary, to operate or train users to operate the equipment efficiently and correctly.

Development of a focused EHS research strategy

The development of a focused research strategy for the EHS aspects of nanotechnology would provide a 'road map' that supports the generation of data, information and knowledge, all of which are essential for supporting informed risk-management decisions. This knowledge is essential for, (1) identifying the potential exposure scenarios of nanomaterials throughout their life cycles, (2) the assessment of nanomaterial impacts on human and other ecological systems and (3) identifying the parameters for the characterisation of nanomaterials, and the classification of nanomaterials in terms of level of potential hazards posed to humans and to the environment.

CONCLUSION

In general, risk assessment of any chemical requires focused research in diverse fields, as illustrated in Table 1. It is important to note that this list is indicative rather than exhaustive. Therefore, it is proposed that a similar approach be adopted for investigating potential nanomaterial risks and that it also serves as a basis to prioritise the most urgent areas of focus as this field evolves. As such, we propose that a team comprising scientists, regulators and industry, as well as other stakeholders, be constituted to refine and define the highest priority areas for research that supports risk-management decisions for nanomaterials in South Africa at the national level. In addition, we emphasise the necessity for periodic or regular reviews of research needs, priorities and strategies. This would ensure that the research conducted at any given time remains relevant and is able to deal with the dynamic changes in the nanotechnology field, both in terms of the new generations of nanomaterials that are being fabricated industrially and the increasing breadth of possible future applications.

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