Environmental, health and safety aspects of nanotechnology—implications for the R&D in (small) companies

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Abstract

The growth of nanotechnology has led to an unprecedented research and development effort in both the public and the private sectors; world wide, an increasing number of laboratories, fabrication and manufacturing plants develop or apply novel nanometre-sized materials for applications ranging from large-scale industrial materials, to electronic components and healthcare and medical products; an increasing number of start-ups have been launched to establish their nanotechnology-based products in a trillion-dollar market.

Very little, however, is known about the interaction of man-made nanostructured materials and living organisms, as studies of nanotoxicology are gaining increasing interest, but are still in their infancy. Despite the formation of many focus and lobbying groups, proper legislation of the environmental, health and safety aspects of nanotechnology will take years to be implemented. In the mean time, it is of utmost importance that companies working with nanometre-sized matter take appropriate precautions to protect their staff, the environment and the customer. Toxicology tests and agency approval of new nanometre-sized materials are prohibitively expensive, but, even if working on a tight budget, nanotechnology companies can achieve an ethical and safe business conduct via a number of possible routes.

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1. Introduction

Nanotechnology is frequently hailed as the next general-purpose technology (GPT) that will impact society in a way similar to that in which electricity and communication technology have become essential in the daily routine of developed countries. The singular term ‘nanotechnology’, however, is inappropriate to describe the vast number of technological innovations based on nanoscale phenomena, and the commercialisation of nanotechnologies is anticipated to outnumber that of previous GPT innovations by several orders of magnitude, as many current GPTs will benefit for nanotechnological advancements. Fig. 1 illustrates the anticipated impact of nanotechnologies on a number of different application areas.

In 2005, emerging nanotechnologies were incorporated into more than US$ 30 billion in manufactured goods (more than double that of 2004), and are forecast to be incorporated into 15% of total global manufacturing output, totaling US$ 2.6 trillion in 2014. [3] In the light of this rapid advancement of often-disruptive nanotechnological innovation, growing concern is raised about the widespread commercialisation of novel materials with largely unknown properties. This has led to an open global debate over the environmental, health and safety (EHS) issues surrounding nanotechnologies, in which public awareness and perception have gained an unprecedented voice of consultation regarding regulation, risk management and acceptance [4].

The removal of genetically modified food from supermarket shelves, brought about by public demand,
demonstrates the importance of a thoroughly conducted public engagement, in which benefits are highlighted, potential risks are debated openly and public concerns are accounted for. Cases of bad working practice, such as the recent hospitalisation of several people who used a glass- and bathroom-sealant spray called ‘MagicNano’, can do serious damage to the entire nanotechnology community by fuelling the repeated calls for a moratorium on nanotechnological research. Nanotechnology companies should therefore conduct transparent and responsible R&D and proactively engage in appropriate toxicology and ecotoxicology test for all nanoenabled products.

2. Discussion

In the last two years, both the public and the private sectors initiated a number of investigations to assess potential EHS risks posed by nanometre-sized materials and to evaluate the technology required to implement adequate risk management strategies.[5–14] The recommendations resulting form these studies raised repeated demands for (a) the implementation of international standards for nanotechnology, (b) the increase of funding for rigorous research the toxicology and ecotoxicology of nanostructured materials,¹ and (c) the publication of nanotoxicological test results [15].

Policy makers in national governments and the governing bodies of international unions (e.g., the European Commission) are now considering the recommendations and are expected to decide on the implementation of appropriate governance. Existing regulatory frameworks covering occupational hygiene and consumer safety are thought to be only partially adequate to govern the manufacture and application of nanoparticles, as they do not account for the phenomena prevailing on the nanometre scale. A number of committees and working parties have been commissioned to investigate the Acts and governing bodies of the regulatory landscape, in order to assess their shared ability to cover all aspects of the required regulation of nanotechnological innovations.

In June 2005, the International Standards Organisation launched ISO/TC 229, a Technical Committee on nanotechnology. It oversees the required standardisations of nanotechnologies, such as classification, terminology and nomenclature, metrology, characterisation, calibration and EHS issues, and consists of representatives from 24 ISO member countries, while an additional eight countries hold an ‘observing status’. It is anticipated that the first set of nanotechnology standards will be published within the next 18 months.²

¹In 2005, the global expenditure on nanotechnologies research and development was US$9.6 billion, of which only US$800 million contributed to research into potential EHS risks.

²Meanwhile, nanotechnology standards are being implemented on the national level: earlier this year, Taiwan introduced the ‘Nano Mark’, a certification system that validates the claims of manufacturers regarding nanoenabled products, and China has published eight national standards governing nanotechnologies.
Nanotechnology companies could therefore soon be asked to match their products to technological standards, but the implementation of clear rules and guidelines for the safe manufacture and application of nanometre-sized materials is anticipated to take a significantly longer time, due to the complex nature of the necessary scientific investigations. In the meantime, the nanotechnology industry needs to adopt proactive risk management strategies, in order to provide a safe working environment for their staff, and, to their clients and customers, products that do not bear health threats at any point of their lifecycle (Fig. 2).

2.1. Risk assessment

For most nanotechnological innovations, the assessment of potential EHS risks is severely hampered by the lack of suitable characterisation equipment and screening processes. In such cases, appropriate safety measures can be recommended only on the basis of models such as ‘quantitative structure–activity relationship’ (QSAR), widely adopted throughout pharmaceutical industry [18]. Some insurance companies have learnt their lesson in asbestos case studies and have applied similar risk approximation methodologies, in order to offer appropriate insurance packages to the nanotechnology industry [19–22]. Even with the backing of complete liability protection, however, the main goal for the nanotechnology industry should always be the minimisation of the risk and the prevention of accidents and incidents in the first place; toxicology tests and exposure measurements of a novel material or substance should be conducted in parallel with its development.

A complete risk assessment includes the evaluation of the exposure (i.e., the concentration of a substance in the medium multiplied by the duration of contact), the dose (i.e., the amount of a substance that reaches a specific (biological) location), the hazard (i.e., the potential of a material to cause harm) and the resulting risk (i.e., the probability of harm occurring as a function of the hazard and dose of a substance and the exposure to the substance. Appropriate environmental, health and safety management should consist of the following steps:

(a) identification of the hazard,
(b) characterisation of a hazard,
(c) assessment of the exposure, depending on different parts of the product lifecycle,
(d) assessment of the risk,
(e) Prevention or control of the risk, and
(f) evaluation of the control measures [7,10].

The decrease of exposure levels is, in many cases, the only means to minimise the risks associated with the use of

3In the US alone, payments to the victims of asbestos-related illnesses have already cost insurers and re-insurers approximately US$ 135 billion and an additional US$ 200–275 billion is expected to be paid after the next round of court rulings, while Australia is witnessing the trial and sentencing of bosses of large development companies, who are accused of continuing to use asbestos long after its detrimental health effects had been proven [20,22].
a hazardous substance, as both the hazard and the dose of a substance are highly dependent on its (physical, chemical, and biological) properties. Almost all nanotechnological innovations rely on the unique properties of one material, rendering it difficult or impossible to replace it by another, even if the latter was proven to be less harmful. In the European chemical industry, however, the new REACH (‘Registration, Evaluation, Authorisation and Restriction of Chemicals’) regulation is about to be implemented; it demands the substitution of harmful substances within 5 years of their registration\(^5\).\(^4\)

In a report commissioned by the UK Government, the Royal Society and the Royal Academy of Engineering recommended nanoparticulate materials to be treated as new substances under the coming REACH regulation, which will eventually supersede the existing notification of new substances (NONS)\(^5\).

2.2. Risk management of known nanoscale materials

Nanoparticulate materials can enter the body via three main routes (Fig. 3):\(^{17,24,25}\)

(a) Inhalation,
(b) ingestion, and
(c) dermal penetration.

The detrimental health effects of inhaling fine aerosols were recognised as early as the 4th century BC,\(^26\) and, since then, various attempts have been made to minimise exposure.\(^5\) While toxicological test of nanoparticles entering through the skin or the gastrointestinal tract are still in their infancy, inhalation toxicology has been concerned with both naturally occurring and engineered nanometre-sized materials for a long time. Most of these studies, however, resulted in contradictory and controversial conclusions, as little or no standardisation of experimental parameters was available. In particular the mass metric, currently applied as a standard in toxicology test, has been found to be unsuitable to explain the high toxicity of nanometre-sized particles; leading nanotoxicology labs, therefore, recommend the adoption of metrics that account for the materials’ active surface area and structure.\(^{24,26}\)

Recent nanotoxicology studies are therefore trying to reach reproducible results by determining the surface effects and other physical parameters of the materials in question. Companies working with nanotechnologies should keep up-to-date with information about the toxicological studies relevant to their area of R&D. A number of institutions are collecting data about ongoing research projects and test results:

(a) The International Council of Nanotechnology (ICON), launched a database for EHS implications of nanoscale materials in 2005, and furthermore, has

\(^{4}\)The new REACH regulation is proposed to be applied to up to 30,000 existing substances, and its implementation is estimated to cost the industry up to € 5.2 billion\(^{23}\).

\(^{5}\)In the 13th century, Edward I prohibited coal burning, in order to minimise the amount of particles in London’s atmosphere—with little effect: by the end of the 19th century, 2 tons of fine soot were released into London’s atmosphere on a daily basis and a dense smog, as the famous Londoner smokierich fog was named in 1905, could kill 500–700 Londoners in a week\(^{27,28}\).
recently funded a survey of nanotechnology best practice in collaboration with the University of California [29].

(b) The Safety of Nano-Materials Interdisciplinary Research Centre (SnIRC) conducts toxicological and epidemiological studies [30].

c) The Woodrow Wilson International Centre for Scholars is conducting a continuing global survey of research projects concerned with the EHS impact of nanotechnologies [31].

d) The Department for Environment, Food and Rural Affairs (DEFRA) in the UK is planning to run a ‘voluntary reporting scheme for engineered nanoscale materials’ and is currently seeking consultation on the proposal of this scheme [32], and

e) The Environmental Protection Agency (EPA) has initiated a voluntary registration program for companies manufacturing nanoparticulate materials [33].

2.3. Identification and characterisation of unknown hazards

Health and safety experts recommend that novel engineered nanoparticles, for which no toxicological data are available, should be treated as new chemicals; this methodology would ensure the maximum protection against exposure, until the true hazardous potential of the substances has been fully characterised. It is, however, desirable to determine the properties of any novel material as soon as possible, in order to facilitate its research, development, manufacture and application in consumer products, and in order to estimate the cost of safety measures at each point of the products’ life-cycle.

The costs associated with necessary toxicological and ecotoxicological studies of novel nanostructured materials can be enormous, and individual nanotechnology companies should not be expected to be the sole bearers of the financial burden, but should be encouraged to participate in funded EHS initiatives made available by governmental organisations and industrial consortia, in order to promote the advancement and commercialisation of nanotechnologies. Such initiatives can be conducted in a number of different ways:

(a) the ‘start-up in safe mode’ model:

The cost for toxicology studies can be accounted for in the business plan of start-ups that are planning to work with nanotechnologies, and arising costs should be included in the fund-raising process.

The founders of Qinetiq nanomaterials, a fully owned subsidiary of the QinetiQ group that specialises in the manufacture of nanometric powders, gave the consideration of EHS implications top priority in the initial assessment of its start-up requirements; nanoparticle exposure levels in the plant were initially determined with borrowed state-of-the art condensation particle counters (CPCs) and scanning mobility particle sizers (SMPSs), and are now being monitored with permanently installed equipment.

(b) The ‘ancient wisdom’ model:

Nanotechnology companies that are created as subsidiaries of larger corporates, can benefit from the health and safety measures and facilities implemented and approved by their parent companies. In the case of nanomaterials subsidiaries that have been created under the wings of large chemicals manufacturers, such as the BayTubes® brand of Bayer, or the Elicarb™ brand created by Thomas Swan, the adopted risk governance strategies often include both the highest safety measures and public engagement efforts that are naturally required from the chemical industry.

Nanotechnology start-ups that have not been founded as part of a larger corporate with experience in EHS risk management, can form similar partnerships at a later stage; C-Sixty Inc., for example, entered a joint venture with Merck & Co., in order to conduct the high risk development of fullerenes-based drugs in collaboration with an experienced, well-equipped member of the pharmaceutical industry [10].

c) The ‘joint-forces’ model:

Companies with interest in nanosciences and technologies can form EHS-specific R&D collaborations with other companies, institutes and public organisations, independent of their sizes, business models, commercial foci or market positions. A recently launched ‘Nanoparticle HS&E Consortium’, consists of more than 14 international partners, such as governmental and nongovernmental organisation, public research institutes, and a range of companies, some of which are direct market competitors. The diverse partnership aims to develop a number of deliverables (including characterisation standards, monitoring protocols, efficiency evaluation of currently available equipment), to determine a ‘best practice’ model for the protection of all workers; the project will be validated in a peer-review process and its findings widely distributed.

Another example of an EHS-focused partnership of unlike partners is the collaboration agreement between DuPont and Environmental Defense, one of the largest environmental NGOs in the US; the joint project aims to create a framework for the responsible development, production, use, and disposal of nanoscale materials.

d) The ‘research-donation’ model:

Companies that cannot afford to enter joint ventures or to second any part of their work force to participate in R&D consortia can sometimes find nanotoxicology research labs, which are grateful for the donation of novel engineered nanometre-sized materials. For example, Dendritic NanoTechnologies Inc. volunteered its materials for review to the Nanotechnology Characterisation Laboratory [10].
The ‘research-collaboration’ model:

One step further than the donation of samples is to start symbiotic research and development projects between companies and research laboratories; such projects enable an interactive assessment of the properties in question and maximise the benefits for both parties. A successful example for this approach is the collaborative development of a new droplet control system (DCS), ventilation scintigraphy technology, and the optimisation of aerosol drug delivery via the lungs (see Fig. 4). This collaboration was conducted by The Technology Partnership and Addenbrooke’s Hospital in Cambridge and it provided valuable insight into the technology of droplet creation and the distribution of different-sized droplets and particles throughout human lungs.

Other examples include the participation of companies like BASF and Oxonica Ltd. in the ‘NanoSafe 2’ programme, a so-called Network of Excellence, funded by the European Commission, whose aim is to develop risk assessment and management for secure industrial production of nanoparticles.

3. Conclusions

The increasing demand for appropriate risk assessment and governance of nanotechnologies affects every organisation involved in the research, development, and commercialisation of products that contain nanoenabled components. Nanotechnology companies must adopt responsible risk assessment and risk management strategies, in order to protect both their staff and clients/customers from the potentially hazardous effects of their products. In cases, for which no appropriate toxicological data are available, maximum risks potentials should be assumed and corresponding precautions taken.

Nanotoxicological research is still in its infancy and the implementation of test standards and commercialisation of appropriate safety control systems can take several years. The advanced understanding of toxicological phenomena on the nanometre scale is largely dependent on technological innovations and scientific results stemming from enhanced R&D in nanotechnologies.

There are a number of ways in which companies, even if operating on tight budgets, can afford to continue the development of their nanotechnological product, while, at the same time, safeguarding the health of their staff and advancing the community’s understanding of nanotoxicological issues; some of these ways were introduced above and demonstrated to be validated working models of ‘good practice’.

In times, where heightened public awareness for negative aspects of scientific and technological innovations represents a welcome target for calls for a moratorium on the commercialisation of nanotechnology-enabled products, nanotechnology companies have a responsibility to improve the public understanding of nanotechnologies, by proactively adopting transparent, ethical working practices, which support the conduct of toxicological and ecotoxicological studies of nanoenabled products.

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