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Nanotechnology: The Next Big Thing, or Much Ado about Nothing?

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Nanotechnology encompasses an increasingly sophisticated ability to manipulate matter at the nanoscale, resulting in new materials, products and devices that demonstrate new and unusual behaviour. While emerging nanotechnologies have great potential for good, there are increasing concerns that the selfsame attributes that make them attractive will also lead to new risks to human health. Research to date suggests that some purposely made nanomaterials will present hazards based on their structure—as well as their chemistry—thus challenging many conventional approaches to risk assessment and management. People involved in making and using these materials need to know what the risks are and how to manage them, if safe nanotechnology-based businesses are to emerge. Yet the challenges faced by the occupational hygiene community in ensuring safe nano-workplaces are substantial. We currently know enough to suggest that some engineered nanomaterials will present new and unusual risks, but there is very little information on how these risks can be identified, assessed and controlled. And many nanomaterials are in production and use now. Good occupational hygiene practices and existing knowledge on working with hazardous substances provide a useful basis for working safely with nanomaterials. But where existing knowledge fails, new research is needed to fill the gaps: this must be strategically administered and targeted to addressing specific issues in a timely manner. Failing to take these steps will ultimately lead to people's health being endangered and emerging nanotechnologies floundering. However, with foresight, sound science and strategic research, we have the opportunity to ensure that emerging nanotechnologies are as safe as possible, while reaching their full potential.

Keywords: aerosols; nanomaterial; nanoparticle; nanotechnology; risk assessment

INTRODUCTION

Nanotechnology is clearly a concept whose time has come. Five years ago, little was known about the technology outside specialist circles. Yet it is now being promoted in the scientific and popular press as a major technological breakthrough, heralding the next industrial revolution. Researchers and developers are talking about how nanotechnology might be used to develop lighter, stronger materials, better batteries and improved solar cells in the near-term (just a few of the many examples), with applications such as targeted cancer treatments, microscopic sensors and even life-mimicking devices in the mid to distant future. This enthusiasm is backed up by serious research and development funding from government and industry—estimated at nearly US$10 billion globally for 2005 (Lux Research, 2006a). At the same time, there are increasing concerns that new nanotechnologies will bring about new risks to human health and the environment, which we are not well equipped to deal with (Maynard, 2006b).

The previous industrial revolution taught us many hard lessons about how rapid technological advances can impact on society. Even so, preventing disease and injury from industrial processes and products with their roots in the industrial revolution still presents many challenges. Relatively recent technologies such as nuclear power and genetically modified organisms have led to increased scepticism within society over the ability of industry and governments to ensure their safety. And the power of people to decide which technologies succeed and which do not—whether based on real or perceived risks—has become a significant factor (Renn, 2005).

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Against this backdrop comes nanotechnology. Early concerns over the possible dangers of an uncontrolled technological advance were voiced by civil society groups such as the ETC Group and Green Peace (Arnall, 2003; ETC Group, 2003). In 2004, the Royal Society and Royal Academy of Engineering published a milestone report addressing the opportunities and potential challenges presented by different nanotechnologies (The Royal Society and The Royal Academy of Engineering, 2004). Since then, a steady stream of reports and papers from groups that include academia, government, non-government organizations and industry have emerged, that consider the dangers of not balancing the benefits of emerging nanotechnologies against potential and novel risks (Hett, 2004; Chemical Industry Vision 2020 technology Partnership and SRC, 2005; Dennison, 2005; EC, 2005; EPA, 2005; Oberdörster *et al*., 2005a; Maynard, 2006a).

Are the promises of nanotechnology and the potential risks real? Or is the current flurry of interest little more than hype? And how should the occupational hygiene community respond—as it represents and protects the first line of people to face possible risks? In short, is nanotechnology the next big thing, or much ado about nothing? To answer these questions, it is necessary to go back to basics and sound science: To ask what nanotechnology is, what evidence for new risks exists, and how we should respond to this evidence.

NANOTECHNOLOGY—A BRIEF OVERVIEW

The celebrated physicist and Nobel Laureate Richard Feynman is perhaps the first person to be credited with having the vision to see the potential of working at the nanoscale. In a lecture at the Californian Institute of Technology in 1959 titled 'There's plenty of room at the bottom', he postulated that being able to manipulate atoms and molecules at will would open up new avenues of technology. In his view:

> The principles of physics, as far as I can see, do not speak against the possibility of maneuvering things atom by atom. It is not an attempt to violate any laws: It is something in principle that can be done; but in practice it has not been done because we are too big. (Feynman, 1959)

Feynman saw the potential for this scale of engineering, but did not have the tools to make it a reality. These came over 20 years later, with the development and application of the Scanning Tunnelling Microscope to moving individual atoms on a substrate. In 1990, Eigler and Schweizer published a now-iconic image of the IBM logo—written on a nickel substrate using just 35 xenon atoms (Eigler and Schweizer, 1990). Ten years later, researchers in the same laboratory demonstrated the ability to construct groups of atoms capable of doing something, using the same technique (Manoharan *et al*., 2000). In this case, they demonstrated the ability to change the electron density at one focus of an elliptical corral of cobalt atoms on a copper substrate, by placing a single atom at the opposing focal point of the ellipse.

Advances in scanning probe microscopy, electron microscopy and other analytical techniques helped to spur on science and technology based around manipulating matter at a near-atomic scale. At a very basic level, this enabled the structure of materials to be probed and explored, and new materials with nanostructure-dependent properties to be developed. Perhaps the best known of the 'new' nanomaterials was carbon nanotubes—discovered in the 1990s (Bethune *et al*., 1993; Iijima, 1991). Single-walled carbon nanotubes (SWCNT) are in essence a single sheet of graphite (graphene), wrapped into a tube $\sim$1.5 nm in diameter (Fig. 1). This unique atomic configuration leads to a material with an exceptionally high strength-to-weight ratio; that is an excellent thermal conductor; that is highly electrically conductive and yet, may be an insulator or semiconductor if the atomic configuration is marginally altered.

Many other materials show unique properties that are dependent on their nanostructure. These range from size-specific fluorescence in semiconductors such as cadmuim selenide due to quantum-confinement, altered optical properties in nanoscale TiO_2 and a whole host of surface area and surface chemistry-dependent behaviours in a wide range of materials. But these are relatively simple nanomaterials. Current research is leading to the development of more sophisticated and heterogeneous materials and devices—based on an increasing ability to engineer in functionality at the nanoscale (Roco, 2004). For instance, multicomponent nanoscale particles are being developed for cancer treatment that will have the ability to attach to diseased cells, enable their position to be tracked, and destroy the cell while leaving surrounding tissue intact when signalled to do so (National Cancer Institute, 2004). Further out, there is interest in replicating biological functions with engineered molecules and systems. For example, researchers at Rice University in Houston have developed 'nano-cars'—four Carbon-60 molecules (the wheels) connected by organic molecules (the chassis), that demonstrate directional motion on a surface (Shirai *et al*., 2005). These are seen as proof-of-concept for 'nanoscale transporters', able to move materials around in a controlled manner at the nanoscale.

Looking further to the future, the idea of building materials and devices from the bottom up—molecule by molecule—has long-been a goal within

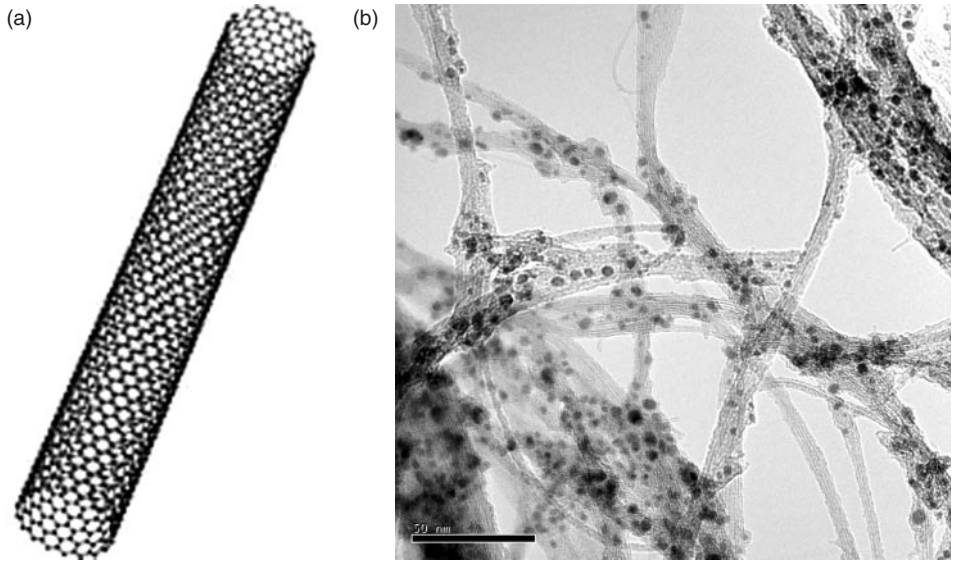

Fig. 1. Single-walled carbon nanotubes. (a) Schematic diagram of a single-walled carbon nanotube © Chris Ewels. (b) Transmission electron micrograph of as-produced single-walled carbon nanotube, showing aligned clusters of nanotubes (nanoropes) and nanometre-diameter metal catalyst particles, used in the production process.

nanotechnology. The idea of 'molecular manufacturing' was explored extensively by Eric Drexler in the 1980s (Drexler, 1986), and is seen by many as a way of mimicking organic systems through nanoscale engineering. Many are sceptical whether it will ever be possible to have such control over atoms and molecules that we can use them to build new chemicals, materials and devices to-order. Nevertheless, the concept has stimulated extensive research. It has also spawned fears of scientists creating a 'grey goo' of self-replicating 'nanobots', which could become an uncontrollable destructive agent. However, these fears would seem to be unfounded in the light of current or even projected developments in nanoscale science and technology.

From this very brief overview, it should be clear that nanotechnology is a concept as diverse as it is nebulous. In many ways, nanotechnology more closely represents a way of thinking or doing things, than a discrete technology. And this makes it particularly difficult to discuss potential risks in general terms. It makes little sense to compare, for instance, the risk to health of an electron microscope (a nanotechnology-based tool) with the risk to health from free SWCNT (a nanotechnology material); or the environmental impact of nano-electronics printing equipment (a nanotechnology-based process) with unbound TiO_2 nanoparticles.

Nevertheless, an informed discussion of nanotechnology and risk must start with some workable definition. The US National Nanotechnology Initiative (NNI) defines nanotechnology as

> the understanding and control of matter at dimensions of roughly 1 to 100 nanometers, where unique phenomena enable novel applications. (NSET, 2004)

In their 2004 report, the Royal Society and the Royal Academy of Engineering were a little more precise, separating out definitions for nanoscience and what they referred to as 'nanotechnologies':

> Nanoscience is the study of phenomena and manipulation of materials at atomic, molecular and macromolecular scales, where properties differ significantly from those at a larger scale.
>
> Nanotechnologies is the design, characterization, production and application of structures, devices and systems by controlling shape and size at the nanometre scale. (The Royal Society and The Royal Academy of Engineering, 2004)

The decision to use 'nanotechnologies' rather than 'nanotechnology' was taken to reflect the diverse and cross-disciplinary nature of the technology.

From the above examples and definitions, it is clear that nanotechnologies have three things in common:

- Control—the ability to put small quantities of matter where it is wanted.
- Utilization—using this ability for some practical purpose.
- Visualization—detecting where material is placed and how it is configured at the nanoscale.

The end result is products that show properties and achieve results that are not possible or easy to achieve with conventional technologies. And this is central to questions concerning new risks: Do these same properties and behaviours lead to new risks; risks

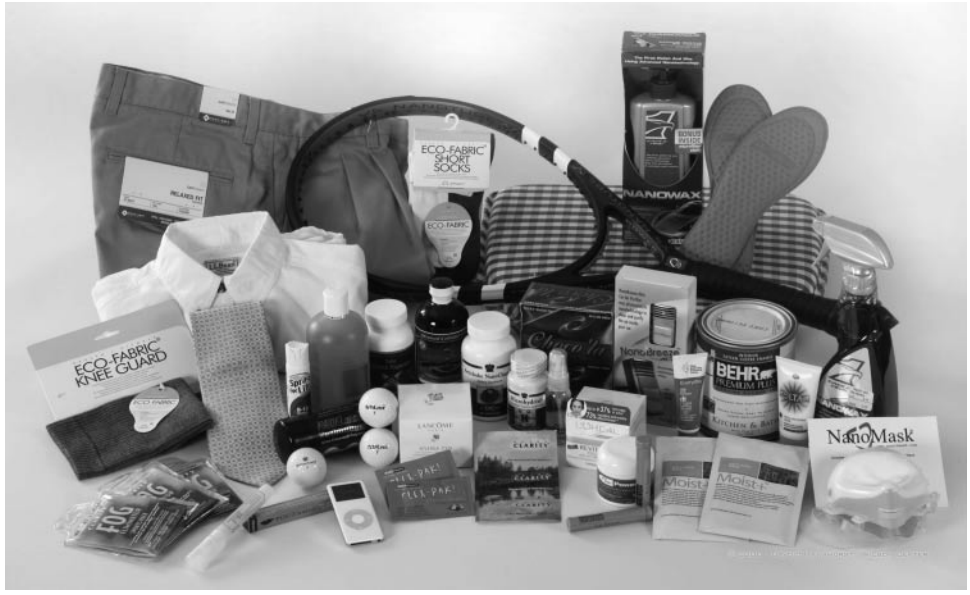

Fig. 2. Examples of current consumer products allegedly using nanotechnology. © 2005 David Hawxhurst, Woodrow Wilson International Center for Scholars (www.nanotechproject.org/consumerproducts).

that perhaps are not adequately identified and managed using current approaches?

This would be something of an academic question if it were not for the rapid and inevitable commercialization of nanotechnologies. Already, investment in research and development has led to over 300 allegedly nanotechnology-based consumer products entering the global market (PEN, 2006) (Fig. 2). These range from computer chips to sports goods and clothing to cosmetics and dietary supplements. And they just represent the visible tip of the nanotechnology iceberg. By 2014, it is estimated that the global value of nanotechnology products will exceed US$2.5 trillion (Lux Research, 2004).

The presence of engineered nanomaterials in the workplace now presents an immediate challenge to how occupational safety and health is managed effectively. A recent report by Lux Research emphasized how important it is for industries developing nanotechnology-based products to address both real and perceived environmental, health and safety risks, if they are to survive (Lux Research, 2006b). And yet, little is still known about what the immediate risks might be, or how to handle them. Still less is known about how we might predict and manage the risks from new technologies in the coming years.

ENGINEERED NANOMATERIALS AND HEALTH HAZARD

While the applications of nanotechnology are incredibly diverse, there is a common thread—a desire to use the scale-dependent properties of nanostructures to enhance existing products, and create new products. There will never be a one-solution-fits-all approach for working safely with nanotechnologies and nanomaterials in the workplace, but this association between structure and functionality provides a useful handle for beginning to explore occupational health risk. The significance of structure—as well as chemistry—in engineered nanomaterials is eloquently demonstrated by the research of Professor Z. L. Wang (Wang *et al*., 2004). Figure 3 shows micrographs of a number of purposely made nanostructured materials. In each case, the chemistry is the same (ZnO), but the physical form is very different. Structure, as well as chemistry, at the nanoscale will determine the behaviour of these materials, in much the same way that both structure and chemistry determine the properties of engineered products at the macro scale—including everything from powders to hand tools to buildings. At the visible scale, it is obvious that structure and chemistry act together to make a product work; the danger is that we ignore the same association when we cannot physically see a nano-engineered material or product.

The concept that both chemistry and structure are important in determining health risk is not new to occupational hygiene: Lung diseases resulting from aerosol exposure are associated with particle size and composition for instance (Maynard and Baron, 2004). In the extreme case, asbestos represents a substance where both chemistry and structure conspire to construct a highly hazardous material in the lungs: change either the composition or the morphology, and the hazard is reduced.

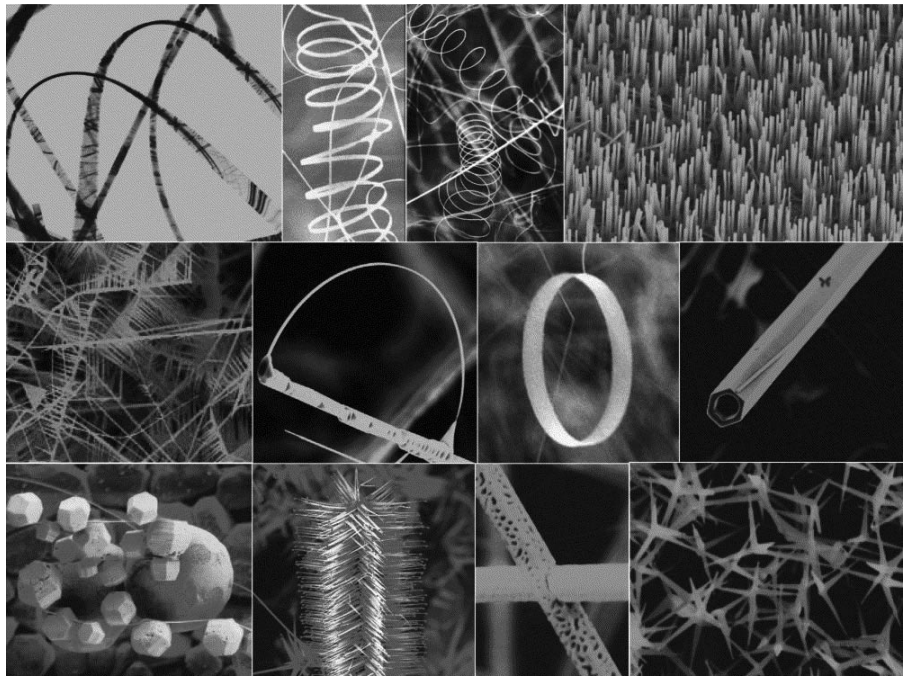

Fig. 3. Examples of ZnO engineered to have different structures (Wang, 2004). Courtesy of Z. L. Wang, Georgia Tech. © 2004, with permission from Elsevier.

If we are to address the potential risks presented by engineered nanomaterials, this concept of structure and chemistry acting together to determine impact needs to be developed and applied. However, a first step is to test its validity. For example, consider the following hypothesis:

> There is a dependency between the physical and chemical structure of engineered nanomaterials and the health hazard they present.

The hypothesis results from the preceding discussion on the significance of structure and chemistry. Without validation, it is little more than an interesting diversion. However, there are published studied that enable us to begin exploring its value.

First, consider the role of particle size—a basic structural parameter of many nanomaterials—and its significance to the potential impact of unbound nanometre-scale particles on health (that is, nanometre-scale particles that are not strongly bound within a solid matrix). Inhaled insoluble particles depositing within the alveolar region of the lungs are typically cleared through phagocytosis and removal up the mucociliary escalator; translocation to the bloodstream or lymphatic system and beyond is not considered a usual clearance path. Does this change at small particle diameters? Kreyling *et al*. have studies nanoparticle translocation from the lungs of rats, using ^{192}Ir particles that are both insoluble and easily traced (Kreyling *et al*., 2002). Introducing 80 nm diameter particles into the animals' lungs, they found a significant mass of material translocating to the liver. However, the translocation rates were low—of the order of 0.1%. When the experiment was repeated with 15 nm diameter particles, translocation rates were significantly higher—between 0.3 and 0.5%. Although still low, the data strongly suggest discrete nanometre-diameter particles can leave the lungs by a non-conventional route.

Looking to another part of the respiratory system, recent research using rodents has suggested that deposited discrete nanometre-diameter particles are capable of being transported from the nasal region of the respiratory tract to the brain, via the olfactory bulb, thus circumventing the blood–brain barrier (Oberdörster *et al*., 2004; Elder *et al*., 2006). While it is by no means certain that this particle size-dependent exposure route is significant in humans, it raises a number of intriguing possibilities when exploring possible associations between exposure and disease.

Staying with particle size but moving to the outside of the body, the skin is traditionally thought of as providing a highly effective barrier against particles. But the inclusion of nanometre-scale particles in cosmetics and sunscreens in recent years has led to this assumption coming under some scrutiny. Most studies support the idea of healthy, intact skin acting as a good barrier—even to nanoscale particles (Lademann *et al*., 1999; Tsuji *et al*., 2006). However, research has demonstrated the potential for submicrometer particles to penetrate the outer layers

of mechanically flexed skin in laboratory tests (Tinkle *et al*., 2003). More recently, 4.6 nm diameter cadmium selenide quantum dots (used for their high fluorescence yield and their well-determined size) have been shown to be capable of penetrating through to the dermis in skin samples (Ryman-Rasmussen *et al*., 2006). But here is the caveat: penetration was dependent on the formulation containing the quantum dots, as well as particle size and possibly shape. In other words, nanometre-diameter particles may be able to penetrate the skin where larger particles cannot, but the probability of penetration will depend on chemistry as well as size.

Moving back to the lungs, research in the 1990s shed important light on the behaviour of nanostructured particles in the respiratory system. Oberdörster *et al*. exposed rats to two different sizes of TiO_2 particles through intratrachial installation, and measured inflammatory response (Oberdörster *et al*., 1994). The chemistry was similar enough between the two particle sizes (25 nm diameter particles and 250 nm diameter particles) to expect the same dose–response relationship as a function of instilled mass in each case. Instead, the smaller nanometre-scale particles were shown to be much more potent for a given mass. Clearly, the response was associated with particle size.

The beauty of these experiments was that, because monodisperse particles were used, the results could be re-examined in terms of different exposure metrics. Plotting inflammatory response as particulate surface area in the rats' lungs—a parameter that is associated with material structure—showed a single dose–response relationship for the two sizes of particle (Oberdörster, 2000). In other words, response was not well-characterized by chemistry alone (represented by mass), but by particle structure (represented by surface area in this case).

Despite clear evidence for an association between inflammatory response and particle structure in this case, it would be naïve to ignore the possible significance of chemistry. What happens if particle surface chemistry is altered—does the hazard potential remain the same, increase or decrease? Comparing inflammatory response to relatively inert insoluble materials such as TiO_2 and $BaSO_4$ to crystalline quartz clearly demonstrates that surface chemistry, as well as structure, has an important role to play (Maynard and Kuempel, 2005). In this case, crystalline quartz is clearly more potent than the same surface area of TiO_2 or $BaSO_4$ in the lungs of rats (Fig. 4).

The final piece of evidence to be considered here addresses the significance of structure in more complex materials in determining biological response in lungs. SWCNT have their own distinct morphology, but also assemble into complex larger structures. Studies examining tissue thickening in the lungs of mice have demonstrated a unique response to purified SWCNT aggregates. But they have also indicated a structure-specific response. Purified SWCNT material introduced to mice through pharyngeal aspiration showed rapid tissue thickening in the proximal and distal regions of the lungs, at doses as small as 20 μg per mouse (Shvedova *et al*., 2005). Histopathology of lung sections using light microscopy identified thickening of granulomatous tissue in the proximal regions with visible compact

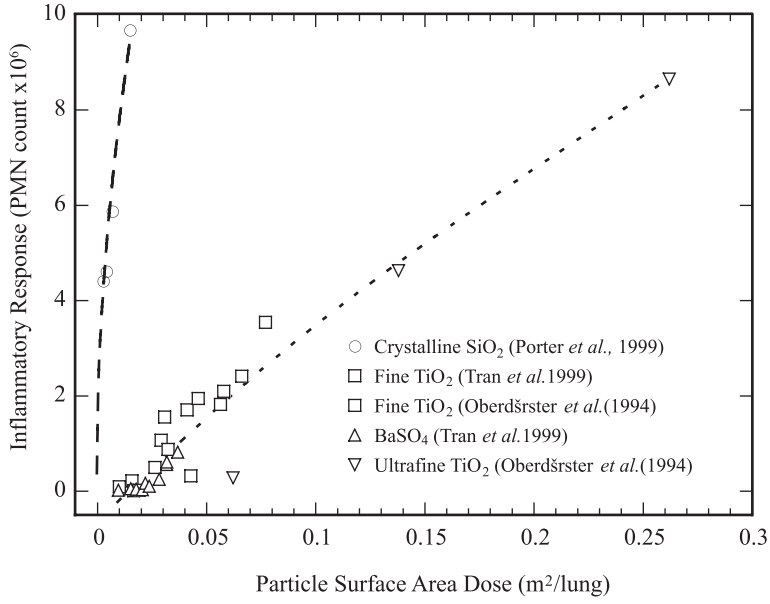

Fig. 4. Pulmonary inflammatory response to crystalline silica (Porter *et al*., 1999), compared with TiO_2 (Oberdörster *et al*., 1994) and $BaSO_4$. (Tran *et al*., 1999). Based on (Maynard and Kuempel, 2005).

SWCNT aggregates; no such aggregates were detected in the distal alveolar tissue, which also showed significant thickening. It now appears that the response in the alveolar region was associated with SWCNT aggregates having a very open structure. Not only were these able to deposit and elicit a response in a different region of the lungs to the compact aggregates: they were not detectable using standard histopathology techniques.

These examples are just a few of many that strongly suggest an association between nanomaterials structure and hazard potential (for instance, see Maynard and Kuempel, 2005; Oberdörster *et al*., 2005a,b; Lam *et al*., 2006). Despite good evidence for such an association, current studies are not conclusive—the range of materials studied is relatively narrow, and some apparently contradictory studies have been published. For instance, Warheit *et al*. failed to detect a significant association between surface area and inflammatory response in rats for a range of TiO_2 particle morphologies and surface chemistries (Warheit *et al*., 2006). Nevertheless, these and other studies do lend substantial weight to the hypothesis that the heath hazard of some engineered nanomaterials will be dependent on chemistry and structure. What published research does not indicate yet is how this potential hazard might relate to risk.

ENGINEERED NANOMATERIALS AND HEALTH RISK

So far, we have a number of 'red flags' that indicate some engineered nanomaterials present a new or unusual health hazard. However, to address possible health impact, we need to understand the risk to human health, and how this might be controlled and managed.

It has already been noted that the diversity of nanotechnologies will most likely prevent a one-solution-fits-all approach to risk. To address risk rationally, nanotechnologies presenting a clear threat to health must be distinguished from those less likely to cause harm. The 2004 report on nanotechnology from the Royal Society and Royal Academy of Engineering (The Royal Society and The Royal Academy of Engineering, 2004) highlighted nanotechnologies associated with unbound sub-100 nm diameter particles as being of particular interest to human health. Oberdörster *et al*. (2005b) support this emphasis on sub-100 nm diameter particles. However, published toxicity studies clearly show that particle size alone is not a good criteria for differentiating between more or less hazardous materials. For instance, inhalation studies using rodents have demonstrated that 20 nm diameter TiO_2 particles had a greater impact on the animals' lungs that pigment-grade particles with the same composition, even though both particle sizes were administered as micrometer–diameter agglomerates (Bermudez *et al*., 2004).

Oberdörster *et al*. (2005a) address the potential health impact of *nanostructured particles*—those having sub-100 nm scale structures—rather than solely focusing on *nanometre–diameter* particles. Maynard and Kuempel (2005) further suggest that the structure-dependent behaviour of nanomaterials indicates an emphasis on nanostructured rather than nano-sized particles. As an example, they consider open agglomerates of SWCNT, which may be micrometers in diameter, but exhibit structure at the nanoscale that is likely to influence their behaviour (Fig. 5).

When addressing inhalation exposure, Maynard and Kuempel propose two criteria for identifying nanomaterials which may present a unique potential risk to human health:

(i) The material must be able to interact with the body in such a way that its nanostructure is biologically available (i.e. exposure must occur, and the material's nanostructure must be biologically accessible following exposure).
(ii) The material should have the potential to elicit a biological response that is associated with its nanostructure (i.e. the potential should exist for a response that differs from that associated a non-nanoscale material of the same composition).

These criteria are inclusive of unbound nanometre-diameter particles (in powders, aerosols and liquid suspensions); agglomerates and aggregates of nanometre—diameter particles—where nanoscale structure-based functionality is retained; aerosolized liquid suspensions of nanomaterials; and the attrition of nanomaterial composites through various mechanisms (Maynard, 2006b).

Under conventional risk assessment paradigms, understanding the risk presented by these materials will be a function of both hazard (incorporating toxicity and health outcomes) and exposure (including exposure routes and dose). There is also a third component that deserves specific attention when addressing engineered nanomaterials: Characterization. Unlike many conventional materials, the relevant characteristics of engineered nanomaterials may be non-obvious, and non-trivial to quantify. In constructing a framework for nanomaterials toxicity testing, Oberdörster *et al*. (2005a) recommend sixteen physicochemical parameters that should be evaluated in toxicity tests—a far cry from the two or three usually measured. These range from surface area and surface chemistry to particle size distribution and particle charge. Engineered nanomaterials are notoriously difficult to characterize—even two materials that are notionally the same may have subtle but significant differences that determine their behaviour.

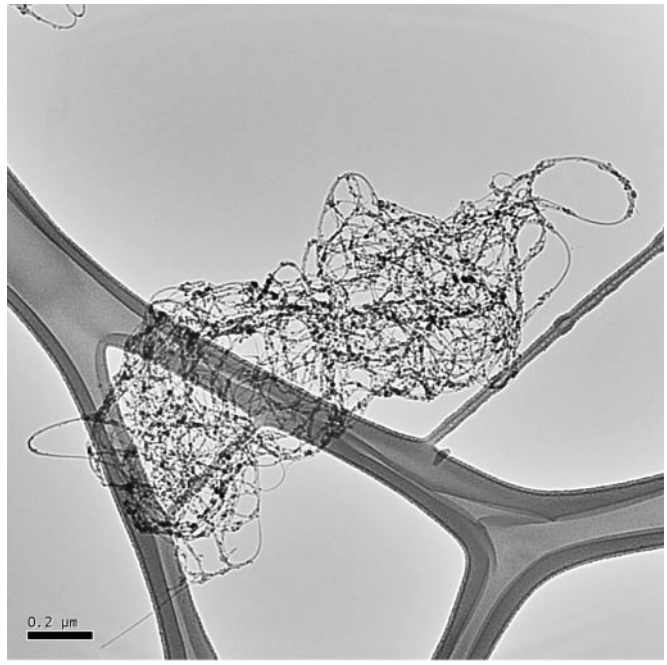

Fig. 5. Transmission electron micrograph of a single-walled carbon nanotube aggregate, held on a lacy carbon support grid. While the aggregate is micrometers in diameter, it is respirable and has a nanostructure that may elicit a response in the lungs if inhaled.

For instance, introducing a small percentage of impurities to the surface of nano-TiO_2 particles may fundamentally alter their propensity to generate free radicals under UV radiation (Wakefield *et al*., 2004). And changes over time such as coagulation, sintering and chemical transformations can likewise alter behaviour. Without rigorous nanomaterials characterization, it will be near-impossible to interpret toxicity studies, compare similar studies and develop predictive models of nanomaterials hazard.

Characterization is just as important for evaluating exposure. In an ideal world, the same parameters of interest to determining hazard would also be used in evaluating exposure. Of course, this would place an impossibly high burden on occupational hygienists. Instead, it is more practical as a first step to consider the three key physical exposure metrics—number concentration, surface area concentration and mass concentration. Oberdörster *et al*. (2005a) and Maynard and Kuempel (2005) conclude that there is still insufficient evidence to preferentially select one exposure metric over another—particularly for airborne exposures—and that where there is uncertainty, all three should be measured.

Measuring aerosol exposure against all three metrics simultaneously is an ideal that still is not achievable, without using costly and bulky equipment. At the same time, it is highly desirable to have some way of measuring exposure to engineered nanomaterials that returns a single value which is relevant to understanding potential health impact. One way of approaching this conundrum is to consider an instrument response that reflects current uncertainty over what should be measured.

At the outset, it is reasonable to assume that the hazard potential represented by an aerosol of nanostructured material is proportional to particle diameter to the power α:

$$\text{Hazard potential} \propto d^{\alpha} \qquad (1)$$

where d is particle diameter. If hazard potential is proportional to mass concentration, α is 3; $\alpha = 2$ if it is proportional to surface area concentration; $\alpha = 1$ if it is proportional to particle length concentration and $\alpha = 0$ if it is proportional to particle number concentration. Assuming no a priori knowledge on which metric is more important, the mean value of $\alpha(\bar{\alpha})$ is $\bar{\alpha} = 1.5$. However, we can be a little more sophisticated in selecting a single but useful value for α: $\alpha = 0$ is likely to be only marginally significant, as this represents a case where there is no dependency between particle structure and hazard potential. Taking the average of the remaining possible values of α gives $\bar{\alpha} = 2$. This is of particular interest, as an instrument conforming to $\bar{\alpha} = 2$ will provide a measure of particle surface area concentration—which seems to be significant for some materials—as well as a possible indication of relevant exposure where the appropriate exposure metric is not known. In other words, an instrument with a response of $\bar{\alpha} = 2$, or between $\bar{\alpha} = 1.5$ and $\bar{\alpha} = 2$, will provide information

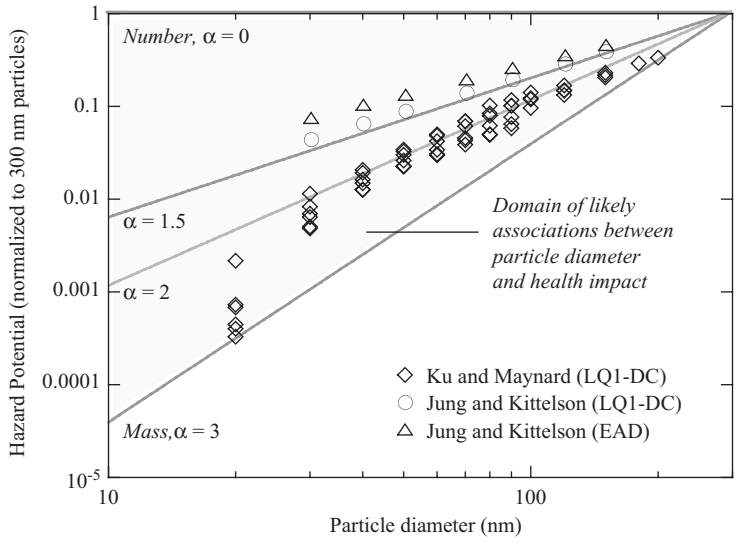

Fig. 6. Possible instrument responses as a function of particle size, for evaluating exposure against airborne engineered nanomaterials (equation 1) (Maynard, 2006b). Also shown are instrument response data on the LQ1-DC (Matter Engineering, Switzerland) and the Electrical Aerosol Detector (TSI Inc., USA) (Jung and Kittelson, 2005; Ku and Maynard, 2005).

likely to be relevant to the potential health impact of airborne engineered nanomaterials.

Figure 6 shows these different instrument responses graphically. Also included are the measured responses of two commercial instruments: the DC2000CE portable diffusion charger (EcoChem, USA) and the Electrical Aerosol Detector (EAD, model 3070A, TSI Inc., USA). Both of these instruments expose the sampled aerosol to positive ions, and measure the charging rate by collecting the particles in an aerosol electrometer. Differences lie in the method used to charge the aerosol and the aerosol flow between sampling inlet and charge detection.

Between 30 nm and 200 nm, the DC2000CE [as characterized by Ku and Maynard (2005)] agrees well with the $\bar{\alpha} = 2$ line. The EAD has a measured response much closer to the $\bar{\alpha} = 1.5$ line [as measured by Jung and Kittelson (2005)]. However, as Jung and Kittelson also measured the DC2000CE as having a similar response to the EAD, there is some ambiguity as to where the precise instrument responses lie.

Despite this uncertainty, diffusion charging is clearly a technology that can provide useful exposure measurements of airborne nanostructured materials. In an interesting development, recent research has indicated the TSI instrument can be adjusted to match the surface area concentration of particles likely to deposit in the lungs by including a tuneable ion trap (Wilson *et al.*, 2004). The resulting instrument—now commercially available as the Nanoparticle Surface Aerosol Monitor (NSAM, model 3550, TSI Inc., USA)—is capable in principle of measuring the surface area of aerosol likely to deposit in either the respirable or thoracic regions of the respiratory system. This opens up the possibility of exploring surface area dose to the lungs rather than exposure. Whether this will be preferable to measuring exposure (or dose-potential) in the long-run is not yet clear. What is encouraging though is that technologies exist that have the potential to be applied to making meaningful nanostructured aerosol exposure measurements.

CONTROLLING EXPOSURE

While developing a sound understanding of hazard and exposure will allow the occupational risks of engineered nanomaterials to be quantified, safe workplaces will depend on controlling exposures. Here there are two challenges: How do we know the efficacy of conventional control approaches for airborne nanomaterials, and how can we define appropriate levels of control if there is insufficient information available for a quantitative risk assessment?

Of these, the second challenge is the more complex of the two to address. Although there are limited data, our current understanding of aerosol behaviour suggests that conventional controls such as local exhaust ventilation, filtration and respirators will be effective for airborne nanostructured particles. However, we are a long way from having enough information on the risks presented by many emerging nanomaterials to evaluate what levels of control are appropriate.

In the absence of good quantitative information, the spectrum of possible responses to controlling nanomaterials exposure is bounded by interpretations of

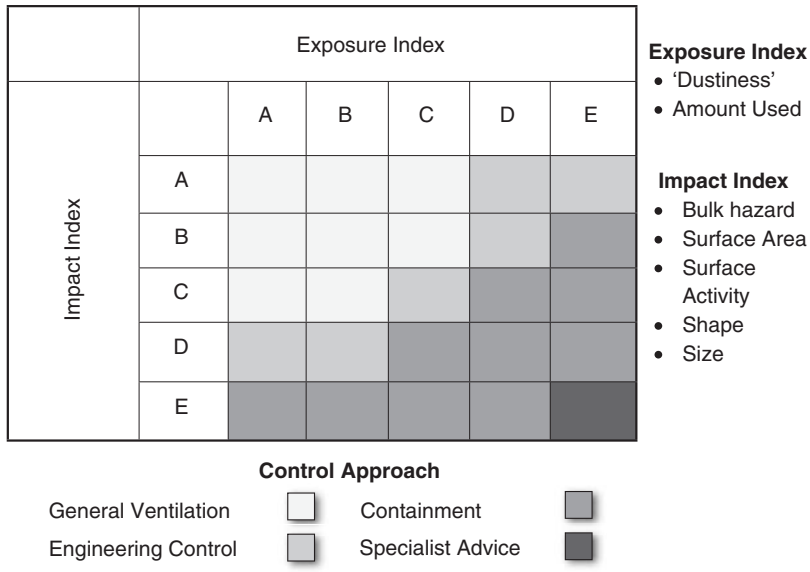

Fig. 7. Conceptual interpretation of how a control-banding type of approach might be applied to airborne engineered nanomaterials.

the precautionary principle at one end, and inaction at the other. The former is typified by an assumption that new materials are highly hazardous until proven otherwise, while the latter assumes the converse: negligible hazard until proven otherwise. Naturally, there are alternative approaches within this range, although in many cases they will require a shift in perspective on how risk is evaluated and managed.

A potentially useful concept that may have some relevance to nanomaterials in the workplace is control banding. Originally developed in the pharmaceutical industry, control banding enables decisions to be made on appropriate levels of control that are product- and process-based, without complete information on hazard and exposure (Oldershaw, 2001; Money, 2003). Rather than being a substitute for conventional risk assessment and control, the concept enables a pragmatic approach to controlling exposure where limited information is available. It is this aspect of decision-making based on incomplete information that is particularly attractive to emerging nanotechnologies and engineered nanomaterials.

The implementation of control banding currently in use through control of substances hazardous to health (COSHH) (Garrod and Rajan-Sithamparanadarajah, 2003) and other systems—which is based on relating material hazard, dustiness and amount used to control approaches—is not directly applicable to engineered nanomaterials. But the concept is. For instance, it may be possible to assign an 'impact index' to engineered nanomaterials, based on their composition-based hazard, and perturbations associated with their nanostructure (for instance, surface area, surface chemistry, shape, particle size, etc.). A corresponding 'exposure index' could in turn represent the amount of material used, and its propensity to become airborne ('dustiness'). As with conventional control banding, the combination of the two indices could then be conceivably linked to specific control bands (Fig. 7).

Of course, this is still very much at a conceptual stage, and would require much more development to make it workable. But it does emphasize the ability to develop non-conventional ways of addressing potential risk that are responsive to emerging nanomaterials, and all of the uncertainties that they represent.

ADDRESSING UNCERTAINTIES

Finally, while we are beginning to develop ways of approaching engineered nanomaterials in the workplace, we cannot avoid the fact that there is an overwhelming level of uncertainty over what materials and technologies present a potential risk, why they do, and how risk might be assessed and managed effectively. In the long-run, safe nanotechnologies will not become a reality unless these uncertainties are addressed systematically. And this means conducting strategic research.

While a number of authors have stressed the gaps in our current knowledge on potential risks, there have been remarkably few attempts to fill these gaps in a systematic way that provides specific answers to specific questions. For instance, a recent report from the Project on Emerging Nanotechnologies in Washington DC (PEN) applauds the actions of the US government in funding risk-relevant research, but points out that there is no overarching

research strategy, and with this, no assurance that the necessary risk-focused research is being done to support nascent nanotechnologies (Maynard, 2006a). The same report sets out a strategic framework for short-term nanotechnology risk-focused research that addresses critical issues.

Immediate priorities highlighted in the PEN report include toxicity testing, measurement methods, control, best practices and research methods. But it is argued that investment in longer-term priorities is also needed now, if we are to build sufficient knowledge and capacity to address future challenges. Identified longer-term priorities include establishing associations between nanomaterials exposure and disease, and developing methods of predicting hazard of new engineered nanomaterials.

To achieve the necessary level of knowledge to support 'safe' nanotechnologies, the report emphasizes the need for targeted research addressing specific and well-defined issues. It also recognizes the need to identify and use risk-relevant research within the broader sphere of nanoscience and nanotechnology. This research, it is argued, must be conducted within and through partnerships if it is to be successful—between researchers, governments, industries and others with a stake in ensuring the safety of emerging nanotechnologies.

SUMMARY

Inevitably, there is a certain amount of hype surrounding nanotechnology—both in terms of what is being promised, and the consequences that are feared. And yet, as an emerging technology, it is not easily dismissed. The term 'nanotechnology' may be a passing fad, but our ability to manipulate matter at the smallest scales will continue to improve, leading to increasingly sophisticated materials and devices that are engineered at the nanoscale. This will continue to open up exciting new possibilities for technologies that can change and improve our lives and the world in which we live. But the same benefits will inevitably bring with them new risks that need to be identified and managed. As people working within emerging nano-industries will be some of the first coming into contact with the new materials, the challenge we face is how to ensure these people remain safe—how to stay ahead of the curve, and assess and manage risk where existing knowledge can only be pushed so far. This is a tough challenge but not impossible. In responding to it, we will first and foremost need to recognize the potential for new risks in some emerging nanotechnologies. We will also need to push existing knowledge as far as it will go in the service of protecting people. Where existing knowledge fails, new research is needed to fill the gaps: this must be administered strategically and targeted to addressing specific issues in a timely manner. Failing to take these steps will ultimately lead to people's health being endangered and emerging nanotechnologies floundering. But with foresight, sound science and strategic research, we have the opportunity to ensure that emerging nanotechnologies are as safe as possible, while reaching their full potential.

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