3.3.2 Monitoring of nanoparticles in the workplace

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Introduction

Nanotechnology is a broad-based enabling technology that holds the promise of major advances in many areas. The next few years will see increasing commercialisation of products that exploit the unique properties of nanoscale materials and devices. However, these same properties present tough new challenges to understanding, predicting and managing potential adverse health effects following exposure. Among the many challenges being faced is the need to be able to monitor exposure to nanomaterials in the workplace in terms of relevant material characteristics. Historically, the mass and bulk chemical composition of materials entering the body have been used to estimate health impact. However, research over the past 15 years has indicated that the size, physical structure and surface chemistry of nanostructured materials play an important role in determining biological response (Donaldson et al. 2000; Oberdörster 2000; Tran et al. 2000; Brown et al. 2001; Oberdörster et al. 2004).

Background

Although nanomaterials may potentially enter the body via a number of routes, most toxicology and epidemiology data related to nanometer-diameter particles to date have focused on inhalation exposure. The potential exists to inhale nanostructured materials when working with suspensions or slurries of nanostructured materials (through sprays and atomisation), nanoscale powders and airborne nanoscale materials. While the composition and chemistry of insoluble inhaled nanomaterials are likely to be important factors in determining biological response, the ability to measure physical characteristics such as size, number and surface-area will be key to appropriate *in situ* exposure monitoring.

A critical step towards developing appropriate airborne exposure monitoring approaches is the definition of particle sizes of interest. Nanotechnology generally refers to the creation and use of sub-100 nm structures, and the exploitation of the unique properties associated with these structures. A wide range of nanostructured materials are formed as powders, suspensions or solutions are comprised of primary particles with diameters of less than 100 nm. Consequently, there has been a tendency to discuss airborne exposure to 'nanoparticles' or 'ultrafine particles' in terms of discrete sub-100 nm diameter airborne particles. However, the unique properties of nanostructured materials are not confined to discrete nanometer diameter particles. In the context of health risk it is important to consider whether the nanostructure of a material leads to a specific or enhanced biological response, and whether the material can interact with the body in such a way that the nanostructure is bio-available. Under these criteria, the size of discrete particles only becomes important where biological activity is associated with individual particles, and where size governs location following inhalation and subsequent translocation in the body. For instance, the increased inflammatory response to ultrafine

TiO_2 reported by Oberdörster *et al.* (Oberdörster et al. 1994) was most likely associated with nanostructured agglomerates larger than 100 nm in diameter (Maynard 2002), and other studies have demonstrated a correlation between surface-area and inflammatory response for particles significantly larger than 100 nm in diameter (Lison et al. 1997; Tran et al. 2000). These and other studies suggest that in some cases nanostructure alone (represented by surface-area) can provide an indication of biological activity. However studies indicating size-dependent particle translocation from the respiratory system to other organs (Nemmar et al. 2001; Nemmar et al. 2002; Oberdörster et al. 2004) suggest that there will be cases where discrete particle diameter strongly influences impact. If particle nanostructure rather than diameter is the primary driver behind biological response, exposure monitoring most likely needs to be carried out with respect to the impacted areas of the respiratory system, in line with the inhalable, thoracic and respirable sampling conventions. However, where discrete particle size potentially drives translocation and biological response, size-selective sampling/monitoring methods beyond these conventions are most likely required.

For an equivalent mass of material, aerosol surface-area varies inversely with particle diameter, and particle number varies inversely with the cube of particle diameter (assuming spherical particles). Thus, even at low mass concentrations, the surface-area and particle number associated with airborne nanoparticles may be substantial. Critical challenges to nanoparticle monitoring include the use of mass-based methods to reflect increasing number and surface-area with decreasing particle diameter, the use of number concentration as an exposure metric and measurement of aerosol surface-area *in situ*.

Monitoring Approaches

Mass concentration measurements offer continuity with historic and current monitoring approaches, but are by their very nature relatively insensitive to nanometer-diameter particles. In principle though, they may offer a bridge between established and new exposure monitoring approaches if high sensitivity and appropriate particle size selectivity is achievable. If particle number or surface-area is a more relevant exposure metric, it may be possible to use mass concentration as a surrogate measurement where information on particle size distribution or aerosol specific surface-area is known.

Aerosol number concentration is relatively easy to measure above 10 nm using Condensation Particle Counters (CPCs), and may be extended to particles as small as 3 nm in diameter with relative ease. Number concentration measurements are generally not size-specific though, unless made with an appropriate pre-separator for a specific particle size range. Consequently, it is difficult to distinguish between different sources of process-related aerosols, or between process and background aerosols. Kuhlbusch *et al.* found number concentration measurements in carbon black production facilities were frequently dominated by other aerosol sources, leading to difficulties in monitoring process-specific emissions using number alone (Kuhlbusch et al. 2004). Despite this drawback, the use of number concentration measurements has been proposed for crude identification of nanometer aerosol emission sources in workplaces by carrying out measurements close to potential or suspected sources (Brouwer et al. 2004).

The surface-area of insoluble nanostructured particles would appear to be an appropriate exposure metric for airborne nanostructured particles, where surface-area and activity are more important than discrete particle size. However, available methods to measure aerosol surface-area are somewhat limited. The Brunaeur, Emmett and Teller (BET) method of determining surface-area remains the standard measurement method for powders (Brunauer et al. 1938), and has been used for aerosol surface-area determination with some success (Lison et al. 1997). However, as well as being an off-line technique, there is little information on how the collection process or particle structure affect the biological applicability of measurements. A second widely used method for determining particle and aerosol surface-area is Transmission Electron Microscopy (TEM). Through the use of image processing, the projected area of sampled particles can be determined with relative ease. Once again though, this is an off-line technique, and the results are open to interpretation.

A number of on-line methods are available for estimating aerosol surface area. The most intuitively obvious perhaps is derivation of surface area from measured size distribution. The association between mobility particle diameter and surface area in the free molecular regime has been well established (Rogak et al. 1993; Ku et al. 2004), allowing size distributions measured using mobility analysis to estimate aerosol surface area reasonably well. To cover an appropriately broad particle size range however, mobility analysis needs to be coupled with techniques such as optical particle sizing or aerodynamic particle sizing. While these techniques are sensitive to particles ranging from a few tenths of a micrometer to tens of micrometers in diameter, assumptions must be made about particle shape and composition to derive surface area. Aerosol surface area estimates have been made in this way (Maynard et al. 2002), but the necessary instrumentation array and the data inversion/interpretation are not typically well suited to routine exposure monitoring.

An intriguing approach to estimating aerosol surface area on line has been proposed by Woo *et al.* (Woo et al. 2001). If an aerosol is assumed to have a unimodal lognormal distribution, the distribution, and hence an estimation of surface area, can be derived from just three independent measurements. Woo *et al.* used measurements of number concentration, mass concentration and aerosol charge to estimate surface area. Estimates made using their method correlated well with estimates derived from size distribution measurements. Recognizing that in many occupational settings aerosol number and mass concentration, but not charge, may be measured simultaneously, Maynard has estimated the anticipated errors that would arise from using just these measurements, and assuming a width for the lognormal size distribution (Maynard 2003). In the worst case, where the sampled aerosol is bimodal, it was predicted that estimates could be wrong by up to a factor of ten. However, simulations showed that in many cases, aerosol surface area estimates from number and mass concentration measurements are likely to be within a factor of four of the actual surface area. Although these errors are potentially large, they may be sufficiently small compared to the range of surface area concentrations experienced to provide semi quantitative banding of exposures.

The first instrument designed specifically to measure aerosol surface area was the epiphaniometer (Baltensperger et al. 1988). This device measures the Fuchs or active surface area of aerosols by measuring the attachment rate of radioactive ions. For particles smaller than approximately 100 nm in diameter, active surface scales as the square of particle diameter, and thus is probably a good indicator of external surface area for nanoparticles. However above approximately 1 μm it scales as particle diameter, and so the relationship with actual particle surface area is lost.(Fuchs 1964). In the transition region there is a gradual shift from active surface area varying as d^2 to d^1. Clearly, if biological impact is associated with geometric surface area, active surface area will underestimate 'biologically available' surface area. However, as the surface area of aerosols comprised predominantly of nanoparticles is dominated by particles smaller than a few hundred nanometers in diameter, it may be that active surface area provides a reasonable estimate of biologically relevant surface area in many cases.

The epiphaniometer is not well suited to widespread use in the workplace due to the inclusion of a radioactive source. However, the same principle forms the basis of diffusion charger-based aerosol monitors where the charging rate is low. Diffusion charger-based aerosol surface area monitors measure the attachment rate of positive unipolar ions to particles, and from this the aerosol active surface area is inferred (Keller et al. 2001). Following charging, usually using a corona discharge, the aerosol is collected onto a HEPA filter within a sensitive electrometer, and the aerosol charge per unit volume of air sampled measured. Evaluation of the LQ1-DC and DC-2000CE diffusion chargers (Matter Engineering, Switzerland) with spherical and fractal-like silver particles show a clear correlation with diameter squared for particles with a mobility diameter below 100 nm. In this region, agreement with TEM and mobility analysis measurement methods is good. Above 100 nm, the diffusion chargers increasingly underestimate the aerosol surface area (Ku et al. 2004).

Although instruments and methodologies for measuring aerosol exposure against a range of metrics are still at an early stage of development, it is currently possible to estimate exposures in terms of surface area and number concentration. The continued testing and development of available techniques will lead to routine exposure measurements of number and surface area that are increasingly viable. In addition, the commercialization of emerging technologies such as personal diffusion chargers, compact integrated mobility analyzers and cross-flow mobility analyzers has the potential to lead to inexpensive, real-time personal samplers over the next few years. However, as these technologies are increasingly used to monitor exposure against a range of metrics, it must be remembered that the measurements only provide an indicator of the potential biological activity of a given aerosol.

If, as is indicated, the health impact of nanostructured materials is related to a combination of physical and chemical properties, measurements need to be understood in the context of the nature of the aerosol being sampled. In the case of measurements such as aerosol surface-area, it is intuitive that these need to be related to the surface activity of a given material. Likewise, the size range of particles to which a particular measurement method is sensitive needs to be considered. As the physical characteristics

of aerosols can change through coagulation and dispersion, care needs to be taken over where measurements are made in relation to generation and inhalation locations. The surface chemistry of nanostructured particles may also be influenced by conditions during transportation, or even by the process of generation. Thus, while it is likely that metrics such as number and surface-area concentration will provide biologically relevant exposure measurements for many airborne nanostructured materials, the validity of these measurements will only be as good as our understanding of their limitations, and the underlying biological activity they represent.

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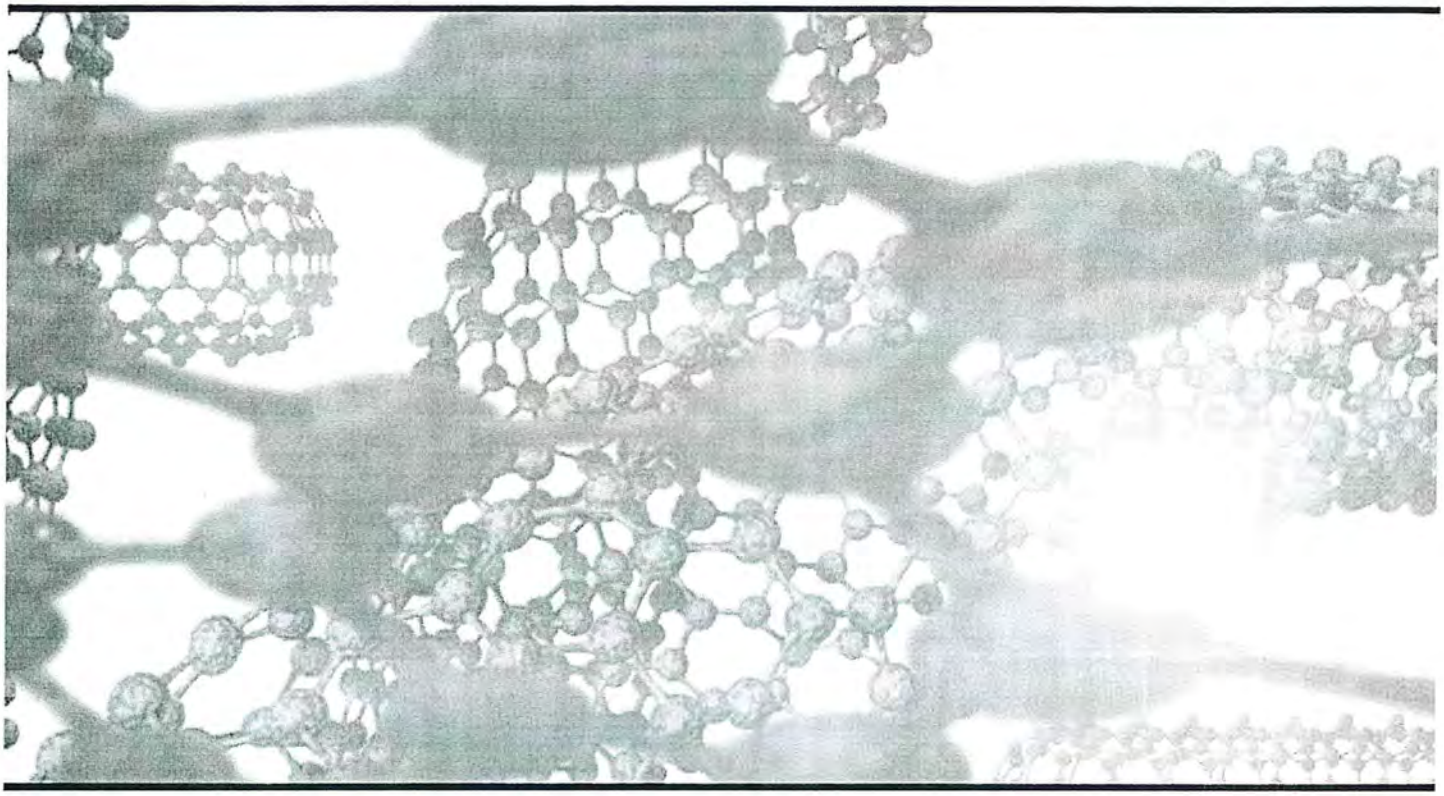
Nanomaterials

a risk to health at work?



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