Editorial

Ultrafine Particles, Nanotechnology and Occupational Health

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The potential health risks associated with nanotechnology have received considerable attention over recent months. Largely based on research into the toxicity of 'ultrafine particles', concerns have been expressed that engineered nano-sized and nano-structured particles released into the workplace will lead to health risks not predicted within current paradigms. Such is the interest in the potentially unique behavior of such particles in the body, that a new discipline of 'nanotoxicology' was recently proposed (Donaldson et al. 2004).

Traditionally, particle size has played little part in evaluating health risk beyond establishing where in the respiratory tract inhaled particles will potentially deposit. Occupational aerosol exposure management is generally based on the assumption that health effects are primarily associated with the mass and bulk chemistry of inhaled material. The mass-based paradigm has been very effective, leading to substantial reductions in respiratory disease with reduced exposures. However, recent research has challenged the robustness of this approach for low-solubility particles.

A number of studies carried out since the late 1980's have been showing a poor correlation between toxicity and mass alone when using relatively insoluble respirable particles. Oberdorster et al. were some of the first to demonstrate a particle size-dependence on toxicity, using titanium dioxide particles of different diameters (Oberdörster et al. 1995): Agglomerates formed from 25 nm diameter particles were found to be significantly more inflammatory than 250 nm diameter particles. Similar results have been seen for other insoluble and chemically relatively inert materials. In each case, toxicity dependence on particle size was removed when dose was interpreted in terms of particle surface area.

Similar studies have shown that toxic response to inhaled micrometer-diameter low-solubility particles scales poorly with mass concentration, but closely with surface area concentration (e.g. Tran et al. 2000). The dose-response relationship appears to be similar for chemically inert materials, suggesting a mechanism associated with the physical nature of the particles. However, insoluble particles that are chemically active, such as crystalline quartz, remain markedly more toxic than other insoluble materials, even when normalized for surface area. Thus for aerosol particles that are poorly soluble, both surface area and surface chemistry are likely to be key factors in determining health risk.

This research clearly implies that insoluble aerosols of very small particles having a high specific surface area are potentially more toxic than those comprised of larger particles. The term 'ultrafine aerosol' has been loosely adopted to differentiate aerosols dominated by sub-100 nm diameter particles from those dominated by larger particles. The definition is somewhat arbitrary, and has relatively little bearing on the surface area-related health impact of aerosol particles. However, recent research has indicated that diameter may have an additional role in determining the fate of deposited particles in the nanometer size range.

Particles smaller than a few hundred nanometers in diameter can be interstitialized following deposition in the lungs (Ferin and Oberdörster 1992), and there is mounting evidence that nanometer-diameter particles can pass from the lungs into the bloodstream and present a systemic health hazard e.g. (Oberdörster et al. 2002). It also seems that particles depositing in the nasal region may be transported to the olfactory bulb via the olfactory nerves (Oberdörster et al. 2004). Although evidence has yet to be presented on particle size-dependent toxicity that goes beyond a surface-area relationship, the potential role of particle diameter in the nanometer size region cannot be ignored.

This increasing body of toxicity data on insoluble and nanometer-diameter aerosol particles raises many questions. Underlying mechanisms determining insoluble particle toxicity and the role of surface chemistry in determining fate and response are still poorly understood. In addition, little is know about how particle agglomeration/de-agglomeration affects dose and biological response, or how these particles should be characterized and controlled in the workplace.

Aerosols that are dominated by nanometer-diameter particles are of particular interest, whether the particles are discrete, or present as agglomerates where the nanostructure is biologically accessible. Many workers are potentially exposed to such aerosols formed as by-products of processes such as welding,

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combustion and metal, or generated while handling mass-produced nano-scale powders such as ultrafine titanium dioxide or carbon black. Furthermore, the increasing commercialization of nanotechnology raises the possibility of workers being exposed to new, unique nanostructured materials.

Heralded by some as the next technological revolution, nanotechnology seems poised to impact on every aspect of our lives. Primarily an enabling technology, nanotechnology cuts across traditional scientific boundaries, leading to new materials, structures and devices that are engineered at near-atomic length scales. By engineering structures on a nanometer length scale, it becomes possible to exploit the unique physical and chemical properties of materials that lie in the 'grey area' between bulk solids and individual atoms and molecules. The vast potential of the technology is reflected in research and development funding: Government funding in 2003 was estimated at nearly $3 billion worldwide (Roco 2003). Nanomaterials and devices promise great potential, including stronger, lighter materials, smaller, lighter, more sensitive sensors, innovative medical imaging and therapeutics and high-efficiency energy storage and conversion.

A number of nanotechnology-based materials are formed or used in the gas phase, and it is inevitable that the technology will lead to some workers being exposed to new and unique nano-sized and/or nanostructured particles. Single walled carbon nanotubes are a good example. Individual single walled carbon nanotubes are relatively insoluble, on the order of 1.4 nm in diameter, up to tens of micrometers long, with a specific surface area in excess of 3000 m2/g. Gas-phase processes generally use transition metal catalyst particles on the order of a few nanometers in diameter during production. The resulting unprocessed material is a matrix of nanotubes (usually in the form of bundles, or nanoropes), nanometer-diameter catalyst particles such as iron or nickel, and carbonaceous material similar to carbon black. Early studies have been inconclusive on the toxicity of the material, although it does appear to be biologically active (e.g. Warheit et al. 2004). However, the material is so unique in our experience that appropriate protocols for testing its toxicity are still being worked out. Carbon nanotubes are just a single example of the new materials that may be encountered in the workplace as nanotechnology progresses.

Nanotechnology offers the promise of many benefits to society. However, it also presents many challenges to how we work responsibly with nanomaterials and devices and protect the health of workers. Fortunately, the research initiated by concerns over exposure to insoluble aerosols has laid a good foundation for addressing critical issues. While we don't have all the answers yet, we can start asking appropriate questions. Sufficient toxicity data are available to raise concerns over exposure to nano-structured materials where appropriate. Measurement techniques capable of monitoring the size distribution and surface area of aerosols are available, and have the potential to be extended for routine use (Maynard 2003). Although little is known about the efficacy of engineering controls, personal protective equipment and respiratory protection for nanostructured materials, accepted and validated theory provides a good starting point for developing appropriate health-related production and handling strategies.

Uniquely, we have an opportunity to develop appropriate risk management systems in parallel with a new technology. If the opportunity is not taken, we run the risk of endangering the health of workers. However, through international collaborations and partnerships among researchers, industry, policy makers and other stakeholders aimed at understanding and controlling the risks associated with exposure to nanoscale materials, we have the potential to facilitate the development and implementation of what has been termed 'responsible nanotechnology'.

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