Nanotechnology

Understanding the occupational safety and health challenges

By John Springston

SINCE 1989, WHEN IBM RESEARCHERS constructed a 35-atom depiction of the company’s logo, nanotechnology has grown rapidly worldwide and is considered by some to be the largest engineering innovation since the Industrial Revolution. Nanomaterials, which are defined as having at least one dimension of 100 nanometers (nm) or less, are formed by molecular level engineering to achieve different and/or enhanced properties, as compared with the same materials at a larger size, due to an increased relative surface area and a dominance of quantum effects on the particles. These properties, which may not even be exhibited by the same materials when they are larger, can include different or enhanced electronic, magnetic, mechanical and/or optical properties. These same properties, however, present new challenges to understanding, predicting and managing potential adverse health effects following exposure (Hood, 2004). Molecular manufacturing of nanomaterials has already found its way into nearly 580 mainstream commercial products and product lines, including clothing, cosmetics and tennis balls (Project on Emerging Technologies). Indeed, the worldwide market for nanotechnology-produced products is estimated to reach $1 trillion by 2015, if not sooner (Roco, 2005).

Many well-known industrial processes unintentionally produce nanometer-sized particles, commonly referred to as ultrafine particles, as part of their process or as by-products. One example is welding, which can generate large quantities of ultrafine particles, usually in the form of a well-defined plume of aggregated nanometer-sized particles. Particles in the nanometer size range are also produced in large quantities from diesel engines, as well as from certain domestic activities such as gas cooking.

Ultrafine particles are present in the ambient atmosphere as a result of combustion sources (such as forest fires and vehicular traffic), volcanic activity and from atmospheric gas to particle conversion processes, such as photochemically driven nucleation (Aitken, Creely & Tran, 2004). The primary particles emitted from the various sources interact in the atmosphere, via chemical reactions, with oxygen, ozone, nitrogen dioxide, sulfur dioxide and organic compounds producing secondary particles that have diverse reactivity and characteristics. The major chemical constituents of these ambient ultrafine particles are typically sulfate, nitrate, ammonium, organic carbon, elemental carbon and a variety of trace metals that are formed in combustion processes (Sioutas, Delfino & Singh, 2005).

Currently available man-made nanoparticle products include nanotubes, nanowires, quantum dots and other nanoparticles, which are being used in electronic, magnetic and optoelectronic, biomedical, pharmaceutical, cosmetic, energy, catalytic and materials applications. Specific areas reportedly producing the greatest revenue for nanoparticles include chemical-mechanical polishing, magnetic recording tapes, sunscreens, automotive catalyst supports, biolabeling, electroconductive coatings and optical fibers (National Nanotechnology Initiative). Some experts say that within the next 10 years nanotechnology could be used in nearly half of all new products on the market, including handheld computers, drug treatments, self-cleaning clothing and paints, environmental remediation agents and renewable energy sources (National Nanotechnology Coordination Office, 2003).

Health Effects: The Good & The Bad

In the medical arena, nanotechnology holds promise for many benefits, but it also is sure to become yet another source for human exposure to nanosized particles. In this case, however, that exposure will be due to man-made nanoparticles, not to those that occur naturally. Several lung diseases related to fine and ultrafine dusts in the workplace have long been known, including pneumoconiosis due to asbestos, cotton and silica, welder’s disease, lung cancer and occupational asthma (Singh & Davis, 2002). Engineered nanoparticles and nanotubes now represent a new class of materials that may become airborne and potentially present a hazard to both workers and consumers.

Medical Applications

One of the more promising applications of nanotechnology involves the development of nanosized tools and materials that will be used to deliver drugs and identify and repair damaged or diseased tissues. Nanoparticles, specifically quantum dots, can be used as probes to form covalent links with mol-}

Abstract: Nanotechnology has grown rapidly worldwide and will likely continue to grow exponentially for the foreseeable future. While nanotechnology holds the promise for numerous benefits, it also will become yet another source for human exposure to nanosized particles—some of which will carry significant safety and health risks. This article examines some positive and negative potential health effects associated with nanoparticles, as well as other safety and health concerns, and possible methods for monitoring and controlling workplace exposures.

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Aggregates formed by low-molecular weight surfactants that resemble many properties of micelles. 

**Nanolong**. A desired property of being able to solubilize both hydrophobic and hydrophilic compounds. 

**Micelles**. Fluid aggregates of a number of molecules that are held loosely together by secondary bonds. Micelles may take on several different forms, depending on the conditions and composition of the system, such as distorted spheres, disks or rods. Micellar systems have the unique property of being able to solubilize both hydrophobic and hydrophilic compounds. 

**Nanometer**. One one-billionth of a meter. 

**Nanoparticles**. Particles of less than 100 nanometers in diameter that exhibit new or enhanced size-dependent properties compared with larger particles of the same material. 

**Phenotypic growth**. A change in cellular characteristics or behavior in response to external agents. 

**Polymer nanoparticles**. A nanosized material constructed of smaller molecules of the same substance that form larger molecules. 

**Polymersomes**. Bilayered membranes of amphiphilic synthetic polymers that are similar to liposomes. 

**Scanning electron microscope (SEM)**. A microscope in which a finely focused beam of electrons is scanned across an object, and the electron intensity variations are used to construct an image of the object. This type of microscope can effectively achieve 200 to 35,000 times magnifications. 

**Transmission electron microscope (TEM)**. A microscope in which a finely focused beam of electrons is transmitted through an object and form a diffraction pattern. This diffraction pattern can then be transformed with a lens to obtain an image of the sample. Magnifications of greater than 1 million times are achievable with modern equipment. 

**Thermal impact**. The impact of particles with a surface as a result of their thermal velocity. 

**Thermal scalpel**. The use of gold nanoparticles, which can turn near-infrared laser light into intense heat, to target and kill tumor cells. 

**Thermal rebound**. The phenomenon of particles bouncing off the surface of a filter material due to their thermal velocity. 

**Thermal velocity**. The speed at which a particular particle travels at a given temperature. 

**Ultrafine**. Nanometer-diameter particles that have not been intentionally produced, but rather are the incidental products of processes involving combustion, welding or diesel engines. 

**Wormlike micelles**. Tubular aggregates that resemble many properties of micelles. 

Perhaps one of the most promising medical applications for nanoparticles is in cancer treatment. Conventional treatments are nonspecific to target killing of tumor cells, can cause severe systemic toxicity and may produce drug-resistant phenotypic growth. The use of tumor-specific nanosized thermal scalpsels to ablate tumors, however, may become a reality. In one animal study, selective photothermal ablation of tumors in mice was performed using intravenously injected polyethylene-coated gold nanoshells with a diameter of ~130 nm. All of the treated tumors were ablated and the treated mice appeared to be healthy and tumor-free more than 90 days later (O’Neal, Hirsch, Halas, et al., 2004). A similar study involving antibody-coated iron oxide nanoparticles with a diameter of ~20 nm showed specific targeted binding to tumors and tumor necrosis 48 hours after injection of the bioprobes (DeNardo, DeNardo, Miers, et al., 2005).

**Adverse Health Effects**

Studies have shown that a large percentage of inhaled nanosized particles—66% ± 12% by number and 58% ± 1.4% by mass—are deposited in the pulmonary region of humans (Frampton, 2001). Several other studies have demonstrated the enhanced ability of ultrafine particles to penetrate more deeply into the lungs than larger particles and to evade clearance (Geiser, Roth-Rutishauser, Kapp, et al., 2005; Oberdorster, Oberdorster & Oberdorster, 2005). Because of their ability to evade clearance, ultrafine particles are retained longer in the pulmonary interstitium which, in turn, increases the potential for translocation to extrapulmonary sites. Indeed, early research has suggested that insoluble nanosized particles in the lungs possibly enter cells and translocate to other organs in the body, including the heart, liver, brain and central nervous system (Takakatsu, Kang, Roti, et al., 2001; Oberdorster, Sharp, Atudorei, et al., 2002; Oberdorster, Sharp, Atudorei, et al., 2004; Elder, Gelein, Silva, et al., 2006).

Animal studies thus far have shown pulmonary inflammation, along with histopathological changes.
and translocation of ultrafine particles to extrapulmonary tissues (Elder, Gelein, Azadniv, et al., 2004; Warheit, Laurence, Reed, et al., 2004; Elder, Gelein, Finkelstein, et al., 2005). The extent to which this process occurs, however, depends on several different factors, including particle size and solubility, the deposition site and the integrity of the epithelial lining.

Translocation of nanoparticles could play a major role in the development of certain cardiac and/or central nervous system diseases, although these phenomena have yet to be clearly demonstrated in humans (Oberdorster, et al., 2005). A study on the association between adverse health outcomes and inhalation of airborne particles and copollutants noted that although the relative risks for effects of particles are greater for respiratory than for cardiovascular deaths the actual numbers of cardiovascular deaths are greater than those due to respiratory causes (Dockery, 2001). The same authors also found an increased risk of myocardial infarction 1 to 2 hours following an elevated exposure to particles smaller than or equal to 2.5 μm, in size (PM2.5), as well as 1 to 2 days after an elevated 24-hour mean PM2.5 exposure.

Agglomerates of insoluble nanoparticles appear to elicit a response in the lungs that is associated with the surface chemistry and surface area of the particles, rather than the more traditionally measured parameters of mass and chemistry. In one animal study conducted by Lam, James, McCluskey, et al. (2004), mice were intratracheally instilled with carbon nanotubes (CNT), carbon black and quartz, then euthanized either 7 or 90 days later for histopathological study of the lungs. The nanotube products induced dose-dependent epithelioid granulomas and, in some cases, interstitial inflammation in the 7-day groups that persisted and were even more pronounced in the 90-day groups. The results showed that on an equal-weight basis CNT were much more toxic than carbon black and can be more toxic than quartz.

Although there is increasing evidence that exposure to at least some engineered nanoparticles can cause adverse health effects in laboratory animals, no such studies involving workers have, as yet, been published. Indeed, in its draft Current Intelligence Bulletin on medical screening of workers who are potentially exposed to engineered nanoparticles, NIOSH (2007a) stated that “insufficient scientific and medical evidence now exists” to even recommend such screening. The agency did, however, recommend that 1) prudent measures be taken to control exposures; 2) hazard surveillance be conducted as the basis for implementing controls; and 3) that established medical surveillance approaches be considered to help assess whether controls are effective and to identify new or unrecognized problems and health effects.

Nanoparticles & Other Safety Issues

Catalytic Effects

Catalysts are substances that improve the rate or selectivity of chemical reactions without themselves being consumed in the chemical reaction. Because nanoparticles have a very large surface area in relation to their mass, they have much higher chemical reactivity and could cause rapid reactions that would otherwise proceed very slowly. In addition, fewer amounts of materials are necessary to achieve the same reaction.

For example, in 2007, Mazda Motor Corp. revealed a new class of catalytic converters that uses 70 to 90% less precious metals, such as platinum, than are required in current devices (Royal Society of Chemistry, 2007). Finally, some nanomaterials may initiate catalytic reactions, depending on their composition and structure, that would not otherwise be anticipated from their chemical composition alone.

Fire & Explosion

Almost no data are available regarding the potential fire and explosion hazards of nanoparticles. While it is unlikely that very small amounts of nanoparticles will create such a risk, larger amounts of combustible powder very easily could. The ability of nanoparticles to become electrostatically charged presents a unique hazard when dealing with such materials because they can potentially become their own ignition source when dispersed into the air (NIOSH, 2007b). Nanoparticles can be raised from a settled layer into the air far more easily than coarser products, and may remain in suspension almost indefinitely.

In addition, as explained in the following section, conventional methods of measuring dust concentrations may give results that are irrelevant and/or difficult to interpret, thereby creating a false sense of security for workers. Dense clouds of some nanosized powders may be virtually impossible to see, even though a similar suspended concentration of the same material, but at a coarser grade, can be readily visible.

Any nanoparticles that are composed of combustible materials are likely to pose a fire and/or explosion hazard, if present in sufficient quantities or concentrations. The actual explosive concentrations are dependent on the composition of the dust, the particle size distribution and the method of determination, but typical values are around 50 to 100 g/m³ for the lower explosive limit and 2 to 3 kg/m³ for the upper limit (Pritchard, 2004).

Monitoring for Nanoparticles

Historically, monitoring for airborne particles has typically involved sampling to determine the mass and bulk chemistry of the contaminant of concern, either as the total mass or as a respirable fraction of the total. Research on nanoparticles, however, indicates that such mass-based measurements may be less important than particle size, surface area and...
Real-time direct-reading measurements of nanoparticle concentrations are currently limited by the sensitivity of the instrument to be able to detect very small particles.

Particle Mass

Studies indicate that the toxicity of nanoparticles is more associated with the surface area and number of particles rather than with the total mass of the aerosol. Because of their extremely small size, nanoparticles contribute little to gravimetric measurement of exposure levels. However, mass concentration measurements may be appropriate for determining occupational exposures to nanoparticles where a good correlation exists between the surface area of the particles and the mass concentration. Air samples can be collected using inhalable, thoracic or respirable samplers, depending on the region of the respiratory system that is most susceptible to the inhaled particles. Based on current information, the gas-exchange region of the lungs appears to be most susceptible to nanoparticles, which suggests that the use of respirable samplers is most appropriate (ICRP, 1994).

Although respirable fraction samplers allow certain mass-based measurements via gravimetric and/or chemical analysis, they do not provide any information regarding the number, size or surface area of the particles sampled unless the relationship between the various metrics has been previously characterized. No commercially available personal samplers currently available are designed to measure the particle number, surface area or mass concentration of nanosized aerosols.

Conventional size-selective personal impactor designs are limited in their ability to assess nanoparticles since their practical impaction limits are in the range of 200 to 300 nm. Low-pressure cascade impactors can measure particles down to around 50 nm; however, their size and complexity make them unsuitable as personal samplers. In the absence of any specific exposure limits or guidelines for nanoparticles, respirable samplers can be used to gather data on routine exposures from various processes and job tasks. The detection limits for cascade impactors, however, are on the order of a few micrograms per filter or collection substrate, which may make them impractical when sampling for nanoparticles due to their low mass-to-number ratio. Samples collected on appropriate media can subsequently be analyzed via electron microscopy (SEM and/or TEM) to characterize captured particles according to their structure, size and morphology.

Particle Concentration

Real-time direct-reading measurements of nanoparticle concentrations are currently limited by the sensitivity of the instrument to be able to detect very small particles. Most real-time aerosol mass monitors used to assess workplace exposures depend on light scattering from groups of particles in order to determine concentrations. However, this method is generally insensitive to particles smaller than 300 nm. The scanning mobility particle sizer (SMPS), which is a real-time size-selective instrument that can detect particles from around 3 to 800 nm in diameter, is widely used by researchers to characterize nanometer aerosols. However, due to their size, cost and inclusion of a radioactive source, their use in determining workplace exposures is severely limited.

The electrical low-pressure impactor (ELPI) is another real-time measurement instrument for determining particle size-selective number concentrations. The particle number concentrations in individual impactor stages are determined by drawing the collected particles through a corona charger before they enter the impactor, then by measuring the current carried by these particles onto the electrically insulated impaction plates using sensitive electrometers. A 13-stage low pressure impactor (LPI) classifies the particles in different aerodynamic diameter sizes, ranging from about 30 nm up to 10 µm, and each charged particle that impacts a stage is detected. In addition to its aerodynamic size classification characteristics, a major advantage of the ELPI is that it actually collects the various particle fractions, thereby allowing gravimetric or other analysis of the materials (Brouwer, Gipsbers & Lurvink, 2004).

Particle Surface Area

Few methods exist to monitor exposures with respect to the surface area of aerosols, and each method can yield different results. Most methods are based on the isothermal adsorption of nitrogen, and either a single point or a multipoint method is then used to calculate the surface area of the particulate material. Most of these methods, however, require a relatively large amount of material and the measurements are influenced by both particle porosity and adsorption gas characteristics.
One possible interim solution is to estimate surface area based on measurements of particle number and mass concentration using direct-reading instruments. Then, by assuming a lognormal aerosol size distribution with a specific geometric standard deviation, the number and mass concentration measurements can be used to estimate the surface area concentration associated with the distribution (Maynard, 2003).

**Particle Counts**

Numerical aerosol particle concentrations can be measured relatively easily using handheld condensation particle counters (CPC). These instruments are generally sensitive to particles ranging from around 10 nm in diameter up to about 3,000 nm; they can be used in conjunction with an optical counter to determine particle concentrations between the lower CPC detection limit and that of the optical counters (200 to 300 nm).

One drawback with particle counts is that the importance of a particle number concentration with regard to toxicity has not been clearly established. Another critical issue is the fact that nanoparticles are ubiquitous in many workplaces from various other sources such as vehicle emissions, combustion and infiltration of outdoor air (NIOSH, 2006). In one study, where researchers were measuring aerosol exposures during bagging operations involving carbon black, peak aerosol number concentrations were found to be associated with emissions from forklift trucks and gas burners in the area, rather than with the process that was under investigation (Kuhlbusch, Neumann & Fissan, 2004).

**Exposure Control of Nanoparticles**

Because limited information is available regarding potential health risks of occupational exposure to nanoparticles, controls need to be specifically tailored to the various job tasks and processes where exposure may occur. Specific details that need to be considered include the amount of material released into air; how the material’s physical and chemical properties may change while in the air; the likelihood of the material to be inhaled; and the effectiveness of control measures to prevent inhalation (Tsuij, Maynard, Howard, et al., 2006). For example, in one study, the handling of CNT resulted in very low airborne concentrations of nanoparticles, which is consistent with the tendency of this material to aggregate into larger, nonrespirable masses (Maynard, Baron, Foley, et al., 2004).

For most processes and job tasks, it is anticipated that exposures to airborne nanoparticles can be controlled using various engineering controls similar to those currently used in industry (e.g., those used to reduce exposure to welding fumes). Based on what is currently understood regarding nanoparticle motion and behavior in air, control techniques such as source enclosure, fume hoods and local exhaust ventilation systems should be effective in containing and capturing airborne nanoparticles. It is believed that a

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**References**


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Well-designed exhaust ventilation system equipped with high-efficiency particulate air (HEPA) filters should effectively remove airborne nanoparticles (Hinds, 1999). The HEPA filters, however, must be properly seated in well-designed filter housings, otherwise nanoparticles will bypass the filters, resulting in filter efficiencies that are much less than predicted (NIOSH, 2003).

**Nanoparticles & Potential Personal Protection Issues**

**Respiratory Protection**

As with any exposure scenarios, PPE such as respirators should only be used when other control methods are unable to reduce airborne contaminants to an acceptable level. With the exception of supplied-air respirators, they all depend on filtration to reduce the level of contaminants in the ambient air. The particulate filters used in respirators are made of fibrous materials such as fiberglass or polypropylene fibers. As an aerosol navigates through a filter, the trajectories of the particles deviate from the air streamline around the filter fibers due to various well-understood mechanisms. As a result, particles may collide with the filter fibers and become deposited on them.

For larger particles, the removal mechanisms are primarily inertial impaction, interception and gravitational settling. As particle size decreases, filter efficiency decreases until it begins to increase again at around a particle diameter of 200 nm. For particles smaller than 100 nm, Brownian diffusion forces are assumed to become the most important for filtration, and filtration efficiency should increase as the particle size decreases. Brownian diffusion is caused by collisions between particles and the air molecules, thereby creating random paths that the particles follow. The random motion increases the probability that a particle will contact one of the filter fibers. Once the particle is collected onto a fiber, it will adhere to it due to van der Waals forces.

For regular noncharged mechanical filters, such as those typically used in HEPA filters, the peak penetrations occur at a particle diameter of about 300 nm. A numerical model for nanoparticle penetration was suggested which showed that the thermal impact velocity of particles in the size range of 1 to 10 nm will exceed the critical sticking velocity (Wang & Kasper, 1991). Other recent modeling and experiments have suggested the potential for nanoparticles smaller than 2 nm to penetrate filters due to thermal rebound (Ichitsubo, Hashimoto, Alonso, et al., 1996; Kim, Bao, Okuyama, et al., 2006).

Another study, which looked at the penetration of silver nanoparticles ranging in size from 3 to 20 nm through a wide range of filter media and at three different face velocities, found no significant evidence of thermal rebound down to 3 nm (Pui & Kim, 2006). Researchers studying N95 respirators challenged with nanoparticles, however, found that for precharged fiber filters, particles with a diameter range of 30 to 70 nm had the highest penetration values and overall nanoparticle penetration exceeded 5% (Balazy, Ito, Reponen, et al., 2005).

As with filters in local exhaust ventilation systems, the factor which governs the effectiveness of the respirator against particulates is not the absolute penetration through the filter, but rather any leakage(s) that bypasses the filters. By far, the most significant leakage typically occurs at the face-mask seal and is dependent on several factors, including the fit of the mask to the face, work activity and duration of wear. Because of their extremely small size, it is expected that airborne nanoparticles will have high mobility and, therefore, will increase leakage around the mask-to-face seal, although it would not be any more than would be expected for a gas (Aitken, et al. 2004).

**Dermal Protection**

Skin is an important barrier, protecting against insult from the environment. The skin is structured in three layers: the epidermis, the dermis and the subcutaneous layer. The outer layer of the epidermis, the stratum corneum (SC), covers the entire exterior of the body and only contains strongly keratinized dead cells that are glued together by lipids. Depending on the part of the body, the thickness of the SC varies from 0.05 to 1.5 mm. For most chemicals, the SC is the rate-limiting barrier to percutaneous absorption (penetration).

The literature on the ability of nanoparticles to penetrate the skin is limited. As of yet, no evidence has been offered that particles which penetrated the skin had also entered the circulatory system (Hoet, Bruske-Hohlfeld & Salata, 2004).

However, based on the current literature, several suppositions can be made. First, penetration of the skin barrier is size dependent and nanosized particles are more likely to enter more readily and deeply into the skin than larger ones. Second, different types of nanoparticles, such as quantum dots and fullerenes, are more likely to enter more readily and deeply into the skin than larger ones. Second, different types of nanoparticles, such as quantum dots and fullerenes, are more likely to enter more readily and deeply into the skin than larger ones. Third, nanoparticles, such as quantum dots and fullerenes, are more likely to penetrate the skin barrier than do other nanoparticles (Ryman-Rasmussen, Rives, & Monteiro-Riviere, 2006; Rouse, Yang, Ryman-Rasmussen, et al., 2007). Finally, materials that can dissolve or leach from a particle (e.g., metals) or that can break into smaller parts can possibly penetrate the skin (Hostyn, 2003; Verma, Verma, Blume, et al., 2003).

Based on current understanding of the various processes by which nanoparticles can be synthesized, it is highly likely that dermal exposure to nanoparticles will occur in the workplace. Therefore, it may be necessary to introduce some type of dermal protection in order to exclude or limit the amount of exposure that is likely to occur. Latex and nitrile gloves are the most common types of protective gloves worn for protection against nanoparticles, although neoprene and cotton gloves are worn in some workplaces.

While nanomaterials will likely bring about tremendous benefits to society, it is also quite likely that at least some of them will pose significant safety and health risks.
Guides are available regarding the chemical resistance, permeation, degradation and breakthrough times for various types of glove materials, but mostly relate to liquid and gaseous chemicals. Very little information is available regarding permeation and penetration by solid particles, particularly nanosized particles. Both latex and nitrile gloves have intrinsic voids that go well beyond the micrometer size range and that become even more pronounced when they are stretched. These voids may possibly be vulnerable to the penetration of nanoparticles if they are used in unfavorable conditions, such as severe wear and tear or in an elongated state (Ahn & Ellenbecker, 2006).

**Conclusion**

While nanomaterials will likely bring about tremendous benefits to society, it is also quite likely that at least some of them will pose significant safety and health risks. At present, the development and marketing of nanomaterials is advancing much more rapidly than the research into their potential hazards and toxicology. Past experience with other “miracle” materials, such as asbestos, demands that caution be exercised when using new substances without fully evaluating their potential health risks. Current research suggests that conventional PPE may not be as effective against nanomaterials as originally believed. Conversely, it is believed that the same exposure controls that are currently employed in industries which inadvertently produce ultrafine particles, such as welding, will also be effective against engineered nanoparticles. Clearly, additional research is needed in both of these areas.

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