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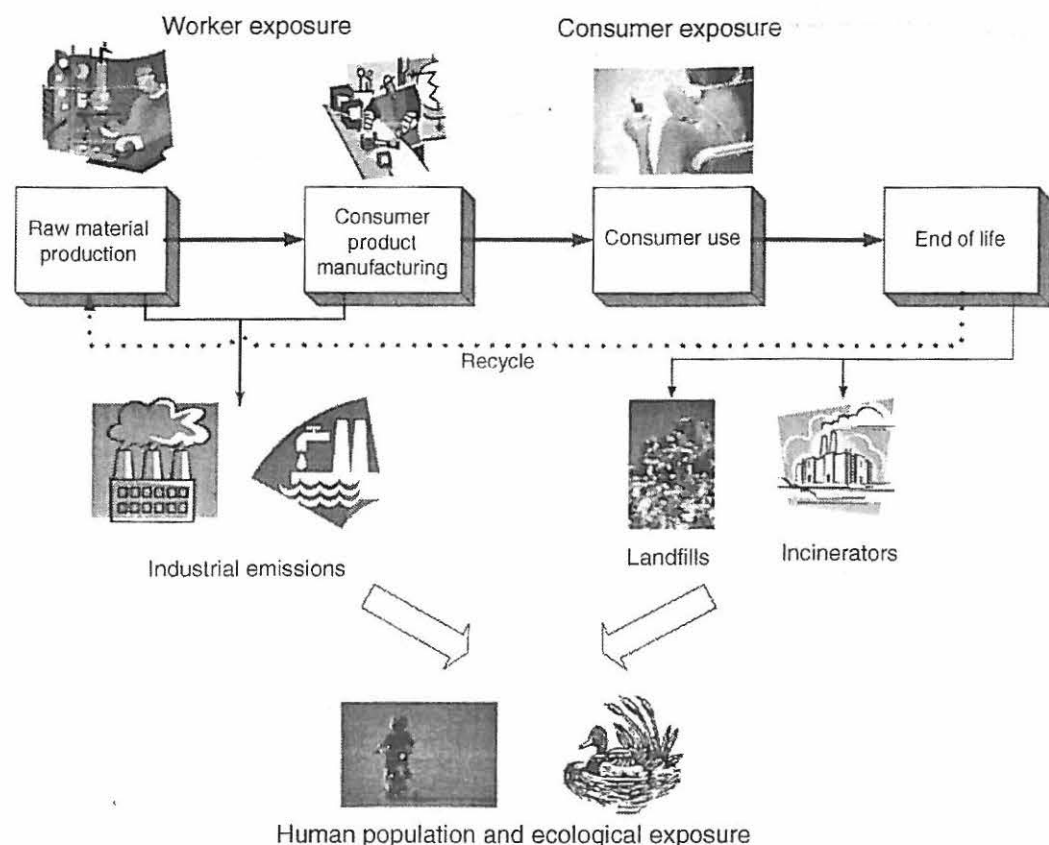
## ENGINEERED NANOMATERIALS

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### 1 INTRODUCTION

Nanoscience and nanotechnology offer new opportunities for making novel engineered materials with improved properties that can be used in numerous products for a wide-range of applications. These materials range from cesium oxide nanoparticles that serve as catalysts for combustion in diesel fuel (1) to silver nanoparticles that provide socks with antibacterial and antifungal properties (2). Nanomaterials are also used to remediate contaminated drinking water and soils, to strengthen materials, and to provide protective coatings on windows and other surfaces. Substantial public and private funding supports research in the production of new engineered nanomaterials due to their promise to enable novel applications that can impact our everyday lives in positive ways.

As research and production grows, it is easy to surmise that workers will increasingly come in contact with engineered nanomaterials (3–5). Each step in the life cycle of a nanomaterial represents a potential exposure hazard either for workers or for consumers (6). Production of a nanomaterial involves any of a number of processes, such as flame-based powder generation used to produce carbon black, nanoscale titanium dioxide, fumed alumina, and fumed silica powders (3). As depicted in Figure 10.1, nanomaterials must be produced, handled, and manipulated to integrate them into consumer products, and most products eventually return to recycling centers. Each step in this life cycle represents the potential for exposure of consumers and/or workers to the nanomaterial (6).



**FIGURE 10.1** Life cycle risk assessment for human and environmental exposure to nanomaterials (6). (Reprinted from Ref. 6).

These materials are potentially different from more common nanoparticles that are incidental to industrial processes (e.g., diesel fumes in mines and metal oxides in foundries) (3). The same properties that make engineered nanomaterials unique and promising for a wide variety of applications may also render them uniquely hazardous to health when they are inhaled, come in contact with skin, or are ingested (7). Toxicity data are available for only a small subset of engineered nanomaterials that are in use today, although this list is growing. These data in some cases suggest that current regulatory workplace standards may be inadequate to protect workers when they produce, handle, or manipulate engineered nanomaterials (7).

It is therefore the environmental health and safety (EHS) professionals whom are responsible for protecting workers that encounter nanomaterials in occupational settings and are in many ways at the frontier of industrial hygiene. Not only are the nanomaterials themselves rapidly evolving but also are the processes that are used to produce them. Unlike most of industrial hygiene that was codified during the early twentieth century, there are no well-tested protocols for evaluating exposures and occupational exposure limits (OELs) to compare measurements with. Moreover, the incredible structural and compositional variability of engineered nanoparticles virtually precludes the traditional measure-and-compare-to-the-OEL approach that has been the foundation of much of the field. Instead, the EHS professional must apply a more thoughtful and nuanced approach, an artfulness that is integral to the definition of industrial hygiene.

There are numerous resources that aim to centralize health, safety, and toxicity pertinent on nanomaterials. Table 10.1 lists resources that we recommend as useful for managing occupational health risks presented by the presence of engineered nanomaterials in the workplace at this time. Web site resources are useful for finding up-to-date recent research for particular types of nanomaterials. They also provide a place to find updated material on regulations and guidance documents. Some review articles have provided good summaries of occupational health and safety for workplaces where nanomaterials are present (3–9). However, these resources alone may be difficult to synthesize and apply especially for those new to the field without some general background information.

**TABLE 10.1 List of Key Resources for Managing Occupational Health Risks for Engineered Nanoparticles**

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***Reports***

Approaches to safe nanotechnology (4)

NIOSH guidelines

[www.cdc.gov/niosh/topics/nanotech/safenano/](http://www.cdc.gov/niosh/topics/nanotech/safenano/)

Workplace atmospheres—ultrafine, nanoparticle, and nanostructured aerosols—inhale exposure characterization and assessment (3)

International Organization for Standards (ISO) statement

Nanoparticles: an occupational hygiene review (5)

overview of industrial hygiene in context of engineered nanomaterials

[www.hse.gov.uk/research/rrpdf/rr274.pdf](http://www.hse.gov.uk/research/rrpdf/rr274.pdf)

***Journal Articles***

Occupational risk management of engineered nanoparticles (9)

industrial hygiene approach to risk management

Nanotoxicology: an emerging discipline evolving from studies of ultrafine particles (8)

overview of exposure, uptake, translocation, and excretion

Human health implications of nanomaterial exposure (7)

detailed review of known biological health effects subdivided by material type

***Web Site Databases***

Good Nano Guide

[www.goodnanoguide.org](http://www.goodnanoguide.org)

National Nanotechnology Initiative (NNI)

[www.nano.gov/](http://www.nano.gov/)

International Council on Nanotechnology (ICON)

[icon.rice.edu/research.cfm](http://icon.rice.edu/research.cfm)

Nanotechnology Risk Resources

[www.nsec.wisc.edu/NanoRisks/NS--NanoRisks.php](http://www.nsec.wisc.edu/NanoRisks/NS--NanoRisks.php)

InterNano Production and Products Database

[www.internano.org/](http://www.internano.org/)

Environmental Protection Agency

Toxic Substances Control Act—[www.epa.gov/oppt/nano/](http://www.epa.gov/oppt/nano/)

SafeNano

[www.safenano.org/](http://www.safenano.org/)

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Hence, this chapter is motivated by the need for a general overview to help the EHS professionals as well as occupational health researchers new to nanotechnology address the many challenges posed by the presence of engineered nanomaterials in the workplace. First, we present a general overview of nanotechnology that includes important definitions, a description of important properties of nanomaterials that may be relevant to health, and an overview of industries where nanomaterials are currently found. Then we present a strategy for addressing the risk posed by nanomaterials in the workplace that is organized on the principles fundamental to industrial hygiene: anticipation, recognition, evaluation, and control. Finally, we discuss the future outlook of industrial hygiene as it relates to protecting worker health in the context of nanomaterials. The intent here is that this overview will serve as a general starting point. Throughout the chapter, we provide numerous references for the reader interested in seeking more detailed information.

## 2 NANOSCIENCE AND NANOTECHNOLOGY

### 2.1 Fundamentals

One nanometer (1 nm) is one billionth, or  $1 \times 10^{-9}$ , of a meter. To put this in some perspective, a human hair is approximately 55,000 nm; biological cells are on the order of 1000 nm; features on a microchip are on the order of 100 nm; the width of a DNA base pair is on the order of 2.5 nm; and a chain of ten hydrogen atoms is on the order of 1 nm.

According to the National Nanotechnology Initiative, a program established in fiscal year 2001 to coordinate federal nanotechnology research and development in the United States, nanotechnology is the understanding and control of matter at dimensions between approximately 1 and 100 nm, where unique phenomena enable novel applications ([www.nano.gov](http://www.nano.gov)). Nanotechnology involves imaging, measuring, modeling, and manipulating matter at this length scale, it encompasses nanoscale science, engineering, and technology. Of particular interest in this size regime is the fact that unusual physical, chemical, and biological properties can emerge in materials at the nanoscale. These properties may differ in important ways from the properties of bulk materials and single atoms or molecules: some are better at conducting electricity or heat, some are stronger, some have different magnetic properties, and some reflect light better or change colors as their size is changed. Therefore, nanomaterials, materials with nanoscale dimensions, behave differently than materials of larger dimensions. It can be stated that that even ordinary materials, such as elemental carbon-based materials, can exhibit extraordinary behavior on the nanoscale (e.g., carbon nanotubes). Another very important property of nanomaterials that is of great interest is the fact that nanomaterials have high surface areas, far higher surface areas than similar volumes of larger scale materials. The higher the surface area the more surface is available for interactions with other materials around them.

This new field has required standardization of vocabulary that is sometimes inconsistently used, especially in occupational health. We therefore recommend



the use of standard vocabulary adopted by the American Standards for Testing and Methods (ASTM E-2456-06) (10), which includes the terms

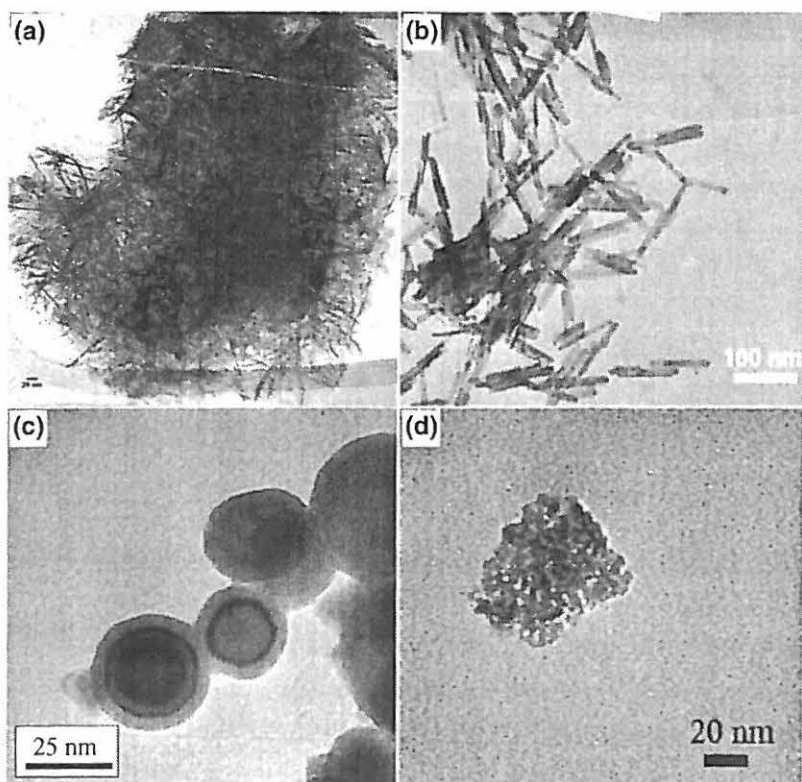
- agglomerate —a group of particles held together by relatively weak forces (for example, van der Waals or capillary) that may break apart into smaller particles upon processing, for example.
- aggregate —a discrete group of particles in which the various individual components are not easily broken apart, such as in the case of primary particles that are strongly bonded together (for example, fused, sintered, or metallically bonded particles).
- fine particle —a particle smaller than about 2500 nm and larger than about 100 nm in size.
- nanotechnology —a term referring to a wide range of technologies that measure, manipulate, or incorporate materials and/or features with at least one dimension between approximately 1 and 100 nm.
- nanoscale —having one or more dimensions from approximately 1 to 100 nm.
- nanoscience —the study of nanoscale materials, processes, phenomena, or devices.
- nanostructured —containing physically or chemically distinguishable components, at least one of which is nanoscale in one or more dimensions.
- nanoparticle —in nanotechnology, a subclassification of ultrafine particle with lengths in two or three dimensions greater than 1 nm and smaller than about 100 nm and that may or may not exhibit a size-related intensive property.
- ultrafine particle —a particle ranging in size from approximately 1 to 100 nm. Generally used to describe those particles found in welding fumes and aerosols that are byproducts of combustion.

Although the term nanomaterial is not uniquely defined by ASTM, the following definition fits in well with the above definitions:

- nanomaterial —a material with structural components between 1 and 100 nm. These components impart unique properties that are not otherwise present in the parent material.

A tendency is to discuss the potential exposure to an engineered nanomaterial in terms of nanoparticles or ultrafine particles (i.e., exclusively those particles smaller than 100 nm in all dimensions). However, nanomaterials often form agglomerates as depicted in images of commercially manufactured nanomaterials sold as powders (images labeled (a), (c), and (d) in Fig. 10.2) and nanomaterials synthesized in an academic laboratory (image labeled (b) in Fig. 10.2). In all cases, the individual primary particles that compose an engineered nanomaterial are nanoscale in one to three dimensions. However, the images in Figure 10.2 also show the great tendency for nanoscale particles to form agglomerates (especially seen in the images labeled (a) and (d) in Fig. 10.2).

Figure 10.3 shows electron microscopy images of airborne particles collected in a workplace that produced metal-oxide nanomaterials (11), in particular a titanium

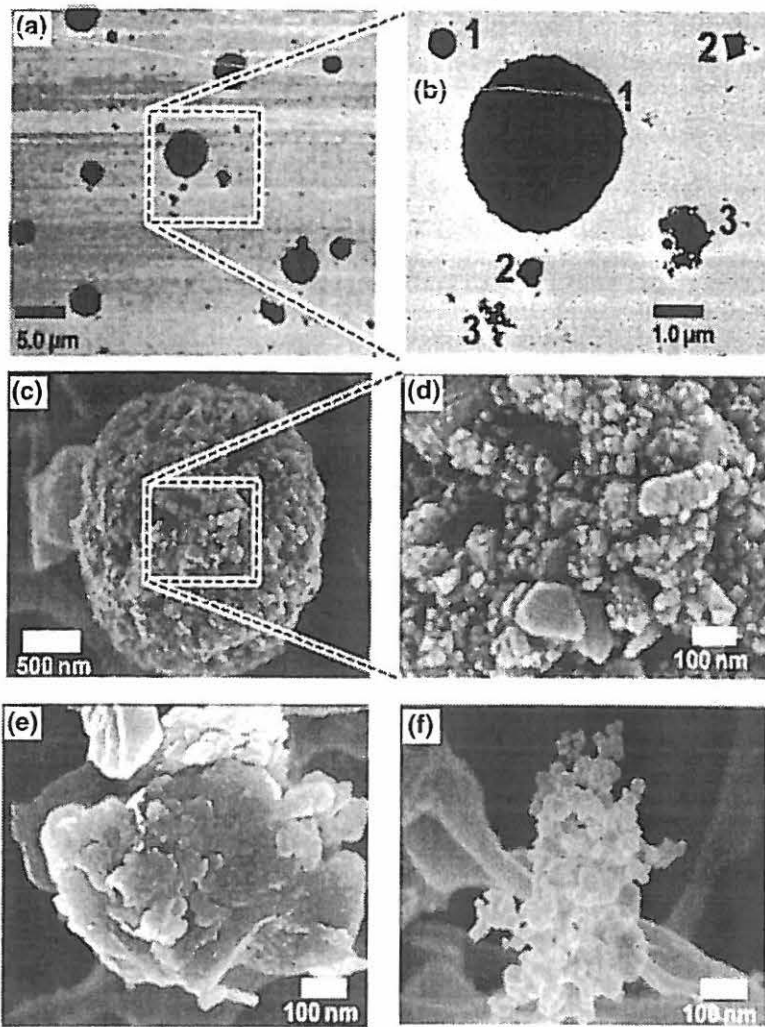


**FIGURE 10.2** Electron microscope images of different nanomaterials with a variety of sizes, shapes, and particle interactions. The upper images show high aspect ratio nanomaterials including aluminum oxide whiskers (a) and iron oxide rods (b). The lower images show spherical particles that are composed of a metallic iron core and an oxidized shell (c) and titanium oxide agglomerates composed of nanoparticles with a primary size below 5 nm (d) (15). (Reprinted from Ref. 15 with permission of John Wiley & Sons, Inc.)

oxide-based nanomaterial. As discussed in detail in Ref. 11, these images when combined with elemental mapping show that airborne engineered nanomaterials can be characterized and classified in terms of their size, shape, and composition. In particular, these images show that the manufacturing of the nanomaterial may be associated with the production of aggregates substantially larger than 100 nm (Fig. 10.3a,b). However, these larger aggregates may still have unique properties imparted by their nanostructure as seen in Figure 10.3c,d. It also shows that incidental nanoparticles or ultrafine particles present in a workplace may be unrelated to the nanomaterial (these particles are shown in Fig. 10.3e,f).

## 2.2 Complexity of Nanomaterials

One of the challenges in addressing EHS issues of nanomaterials, and indeed their scientific fascination, is that engineered nanomaterials can be tuned for specific properties, for example, by changing the size, shape, or the surface coating of the material. A nice example of this is given by gold and silver nanoparticles. In the case of silver and gold, particle size can alter the optical properties of these nanoparticles as



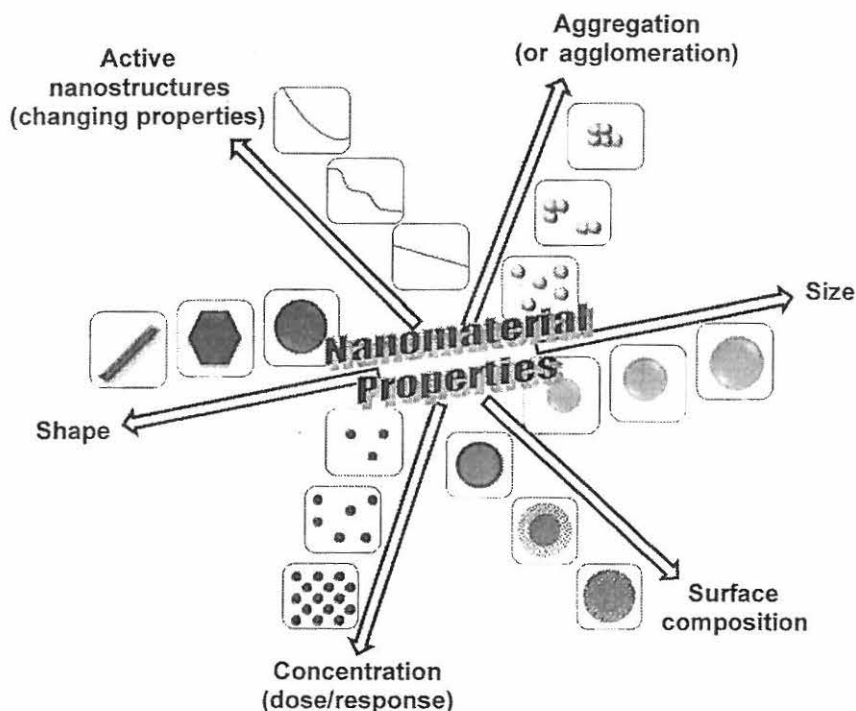
**FIGURE 10.3** Electron microscopy images from filter samples depict a range of particle size and morphologies for particles collected in a manufacturing facility that produces high surface area metal-oxide (titanium oxide) nanomaterials for fuel cell applications. (a) and (b) Transmission electron micrograph images show three types of particles of different shape and size: large spherically shaped particles (1 in (b)); irregularly shaped particles (2 in (b)); and smaller particle chains (3 in (b)). (c)–(e) Scanning electron micrograph images reveal that the larger spherical particles are actually composed of smaller nanoparticles 10–80 nm in size interwoven into larger aggregates ((c) and (d)); irregularly shaped particles have an amorphous structure (e); and chain agglomerates are composed of spherical nodules of 5–50 nm in size. Elemental analysis of these particles show that only the larger spherical particles are composed of titanium and therefore are due to the manufacturing of nanomaterials (11). Reprinted from Ref. 11 with permission of Taylor & Francis.)

seen in the color change observed as a function of size (12). Similarly, shape controls the optical properties as well and silver spherical nanoparticles seen as yellow appear blue when in the shape of a prism instead of a sphere (12). This inherent uniqueness of each nanomaterial with small changes in size and shape represents a major challenge to EHS research and practice. Here, a discussion of general properties of engineered nanomaterials thought to be relevant to EHS evaluation of risk is presented followed by

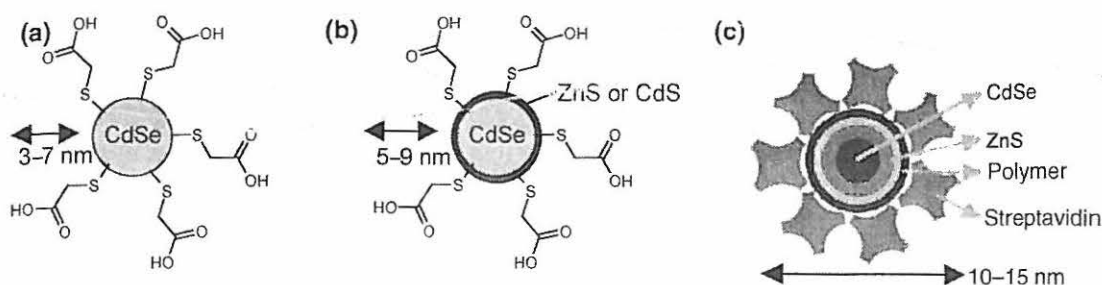
several classification schemes that may be helpful in formulating strategies for occupational risk assessment.

**2.2.1 Properties of Engineered Nanomaterials** Figure 10.4 depicts several properties of engineered nanomaterials that are of fundamental importance to EHS: size, shape, aggregation/agglomeration state, active nanostructures, surface composition, and concentration (13–15). These fundamental properties, in turn, define behavior in water, air, and on surfaces and likely define if or what type of adverse health effect may develop. As the size of an assembly of particles becomes progressively smaller, they become more numerous and have more surface area for a given mass. As discussed above, size may be expressed in terms of the size of the primary nanoparticle or in terms of its aggregation state: primary nanoparticles may be held tightly (aggregated) or loosely (agglomerated). Particle size and shape along with density have important bearing on whether a nanomaterial will be properly controlled for EHS, as, for example, capture and collection in a ventilation system or a respirator (see below for a more complete discussion).

Surface composition plays a key role in the fate and transport of a nanomaterial because many of the atoms in a nanomaterial are in fact at the surface (about 40% for a 4 nm spherical particle). The surfaces of nanomaterials can be functionalized to impart specific behavior. In fact, surface functionalization can impact everything from secondary size (through agglomeration) to water solubility and the ability of



**FIGURE 10.4** Nanomaterial properties vary depending on a number of important characteristics (e.g., shape, concentration (dose/response), surface composition, and aggregation for passive and active (changing) nanostructures (14)). (Modified and adapted from Ref. 13).



**FIGURE 10.5** Chemical composition of the most commonly used quantum dots in biological applications. (a) CdSe quantum dots functionalized with mercaptoacetic acid, whose -SH bonds directly to the semiconductor, leaving the carboxylate group free to interact with aqueous solution. (b) CdSe quantum dots with a 12 nm thick layer of ZnS or CdS, functionalized with mercaptoacetic acid. (c) CdSe/ZnS quantum dots coated with polymers and the protein streptavidin. The overall nanocrystal size is a function of the surface coating and/or functionalization (17). (Reprinted from Ref. 17 with permission of John Wiley & Sons, Inc. Copyright 2008, John Wiley & Sons, Inc.)

nanomaterials to get into cells. As an example, the surface of carbon nanotubes may be oxidized to change them from being hydrophobic to hydrophilic (16). Papp et al. (7) review the considerable effort devoted to understanding the toxicity of hydrophobic carbon nanotubes without an oxidized surface. However, little has been done to characterize hydrophilic nanotubes that potentially have substantially greater mobility in the body. Another example is provided in Figure 10.5 where the surface modification of a quantum dot, a semiconductor nanoparticle (see below) is depicted (17). This figure shows that it is possible to change and modify the quantum dot surface in such a way as to make them useful for biomedical applications and that these surfaces can be functionalized to attach to specific cells in the body.

**2.2.2 Classification Schemes** Several classification schemes are useful in formulating industrial hygiene strategies (18).

**2.2.2.1 Origin** Nanoscale materials in the workplace may have natural origin, be unwanted by products of industrial processes, or be engineered for a particular purpose. Ambient air contains ultrafine particles from natural sources and combustion at concentrations that sometimes exceed those found in industrial settings. These particles may enter the workplace as dilution air in ventilation. Another common source of nanoscale materials in the workplace is the ultrafine particles that result from high-temperature processes such as welding, melting metal, and combustion. These particles are commonly called incidental nanoparticles to contrast them with the engineered nanomaterials that are intentionally produced in or brought into the workplace. Within the context of EHS, it is important to distinguish those materials that are engineered from background ultrafine particles.

**2.2.2.2 Bulk Composition and Structure** Engineered nanomaterials can be made from elemental carbon, carbon-based compounds, metals or metal oxides, and



polymers. Nanomaterials may also be classified by their composition into the following primary groups:

- Carbon-based materials —composed mostly of carbon, commonly taking the form of hollow spheres, ellipsoids, or tubes. Spherical carbon nanomaterials are referred to as fullerenes, while cylindrical ones are called nanotubes. These particles have many potential applications, including improved films and coatings, stronger and lighter materials, and applications in electronics.
- Metal-based materials —include nanogold, nanosilver, and metal oxides, such as titanium dioxide. As already noted above, changing the size of noble metal nanoparticles such as nanogold and nanosilver change their optical properties.
- Semiconductor-based materials —include quantum dots with size-dependent optical emission properties. A quantum dot is a closely packed semiconductor crystal comprised of hundreds or thousands of atoms, and whose size is on the order of a few nanometers to a few hundred nanometers. Quantum dots are often composed of a cadmium selenide core with a zinc sulfide shell. This core-shell motif is very common for quantum dots and the zinc sulfide makes the quantum dots more stable.
- Polymer-based nanomaterials —include dendrimers that are nanosized polymers built from branched units. The surface of a dendrimer has numerous chain ends, which can be tailored to perform specific chemical functions. This property could also be useful for catalysis. In addition, because three-dimensional dendrimers contain interior cavities into which other molecules could be placed, they may be useful for drug delivery.
- Composites —nanoparticles combined with other nanomaterials or with larger, bulk-type materials. Nanoparticles, such as nanosized clays, are already being added to products ranging from auto parts to packaging materials, to enhance mechanical, thermal, barrier, and flame-retardant properties.

It should be noted that a wide array of size, shape, and surface structures are possible even within a single chemical compound.

**2.2.2.3 Free Versus Fixed** Another important distinction relevant to EHS is whether the engineered nanomaterial is free or fixed within the matrix of a larger structure. When not associated with a larger structure, or free, the engineered nanomaterial is available for transfer away from a work area via air or surfaces with relatively little energy input. In contrast, substantially greater forces hold nanomaterials that are embedded within the matrix of a larger structure or substrate bound where they are chemically attached. An example is a drum of carbon nanotubes that will be incorporated into an epoxy composite. Whereas simply opening the drum may offer sufficient energy to disperse carbon nanotubes into the air, some high-energy manipulation (e.g., sanding or machining) may be required to liberate the nanomaterial once it has been incorporated into the composite.



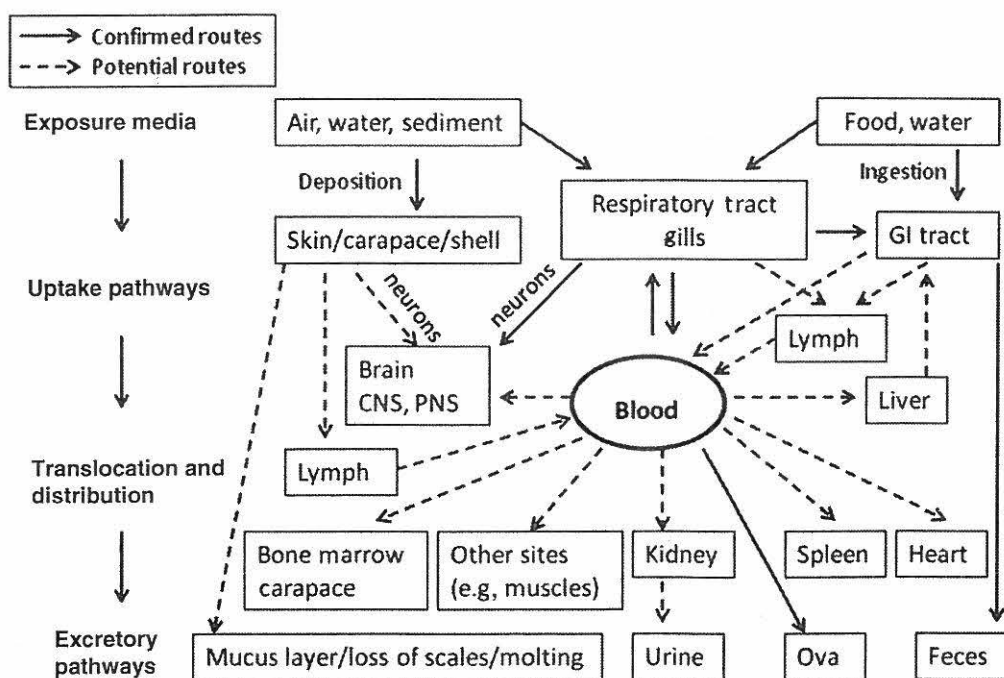
### 3 HEALTH EFFECTS, SAFETY HAZARDS, AND REGULATION

#### 3.1 Health Effects

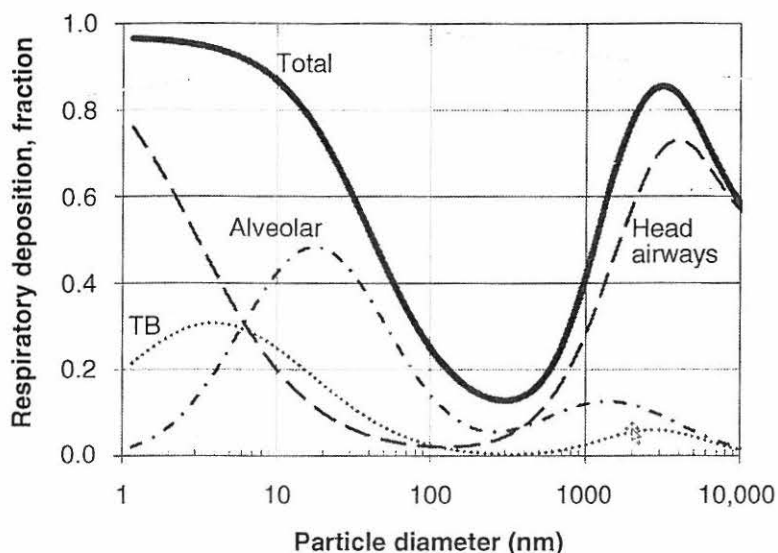
In this section, the health effects of nanomaterials are discussed. In considering health effects, it is important to determine most probable routes of exposure, some of the known safety hazards and a consideration of some of the regulatory processes that are being discussed and under consideration.

**3.1.1 Routes of Exposure** The schematic diagram shown in Figure 10.6 provides an outline of some of the possible exposure routes of engineered nanomaterials. The diagram also shows the possibilities for uptake, translocation, and excretion for these materials. As reviewed by others in detail (7–9), the routes of exposure for engineered nanomaterials are in many ways very similar to other particulates and include inhalation, dermal contact, and ingestion (7–9). Although little is known about the relative magnitude of the different modes of exposure for engineered nanomaterials, inhalation is considered of primary concern for nanomaterials because of the sensitivity of the lung and the ability for nanoscale-sized particles to translocate after depositing into the respiratory system (4).

**3.1.1.1 Inhalation: Deposition** With inhalation exposure, there is concern that nanomaterials can penetrate deep into the lungs. Figure 10.7 presents the empirically based International Commission on Radiological Protection (ICRP) model of fractional deposition of airborne particles in the respiratory system (19). Whereas



**FIGURE 10.6** Schematic diagram of exposure, uptake, translocation, and excretion of nanomaterials in biological systems (8). (Reprinted from Ref. 8).



**FIGURE 10.7** Fractional deposition of particles in the respiratory system by size and region based on the model of the International Commission on Radiological Protection. Average data for males and females for light exercise and nose breathing.

deposition is dominated by gravity settling, impaction, and interception for particles larger than 500 nm (20), it is dominated by diffusion for particles smaller than 300 nm (21). The result is the characteristic dip in overall deposition fraction by size with a minimum for a particle size of 300 nm. The overall deposition of nanoparticles shown in Figure 10.7 has been experimentally verified as generally correct, although the hygroscopicity of the nanomaterial, gender, and respiration rate influence actual deposition (22).

It can be seen from the plots in Figure 10.7 that regional deposition changes dramatically with particle size. Diffusion is thought to cause nearly 100% of 1 nm particles to deposit in the head airways and tracheobronchial region and thus be unavailable for alveolar deposit (19). In contrast for 10 nm particles, only 40% deposit in the upper airways, 50% deposit in the alveolar region, and a small fraction are exhaled. For particles progressively larger than 20 nm, particle diffusion and hence the fraction of particles deposited in each region decreases until other forces become increasingly important larger than 200  $\mu\text{m}$ . Recent computational dynamics models and experiments are generally consistent with the ICRP model, although the exact deposition fraction attributed to each region, especially for particles smaller than 10 nm, is a active area of research (23).

The size, shape, and density of a particle all have bearing on if and where the particle will deposit in the respiratory system. The behavior of straight fibers is more closely related to their cross-sectional diameter than their length because they tend to align with the airflow (24). Carbon nanotubes tend to fold up on themselves when airborne to form low-density tangles (25, 26) and other nanomaterials tend clump to form agglomerates. The concept of aerodynamic diameter, which takes into account size, shape, and density may be used to estimate where these particles will deposit in the respiratory system (20). Generally, the fate of airborne nanomaterials when inhaled

depends on their physical size for primary nanoparticles, agglomerates of nanoparticles, and aggregate nanomaterials with and little is available on the deposition of nanofibers.

**3.1.1.2 Inhalation: Clearance and Translocation** Although the mucociliary escalator can clear nonsoluble particles from the upper airways within hours, clearance of particles from the alveolar region is dominated by macrophage phagocytosis that can take weeks to transpire (27). The efficiency of phagocytosis can be affected by the chemical characteristics of the particle and fibers longer than the diameter of the macrophage can slow phagocytosis (28).

Discrete nanoparticles have been found to evade phagocytosis, translocate from the alveolar region to the blood stream, and be carried to other organs, such as the liver, bladder, and brain (29–32). This behavior is highly size dependent with little translocation observed for 100 nm carbon particles (33) but substantial translocation for 20 nm-sized carbon particles (30).

**3.1.1.3 Dermal Contact** Dermal contact during occupational exposure represents another route for nanomaterial uptake by the body, although data specifically with regard to nanomaterials is sparse and contradictory. Particles smaller than 1  $\mu\text{m}$  may penetrate skin when it is mechanically flexed (34). Studies of quantum dots show deep penetration of the skin is possible depending on the surface coating of the nanomaterial. Other studies found that skin must be damaged by ultraviolet radiation (35) or abrasion (36) before being penetrated by quantum dots.

**3.1.1.4 Ingestion** Ingestion may occur from unintentional hand-to-mouth transfer or as a result of clearance of particles from the mucociliary tract. Inert particles may enter the intestinal tract depending on size, surface charge, ligand attachment, and surfactant coating (37). Generally, the route of ingestion is better characterized than dermal contact. The possible adverse health effects from ingestion of nanomaterials are thought to be minimal because ingestion is a fairly rapid process and the epithelium of this system undergoes a constant renewal process (8).

**3.1.2 Toxicity** Toxicity tests have been conducted on only a few of the multitude of nanomaterials that are currently in use. However, animal studies show evidence that adverse health effects may result in workers from exposure to engineered nanomaterials (7). Generally for a given mass dose of a poorly soluble, low toxicity (PSLT) material, pulmonary inflammatory response and tissue damage is greater if the dose is composed of nanosized particles than larger particles (38, 39). Moreover, surface area rather than mass dose has been shown to more closely scale with the toxic effects of PSLT in the lung (38–42). Some studies have also shown that particle surface area, not mass concentration, may best represents a threshold dose for the proinflammatory effects of low-solubility ultrafine particles in the lung (40–42) and *in vitro* experiments using epithelial cells (39). However, the surface chemistry, crystal structure, and shape of particles appear to affect the dose–response relationship even within one type of nanomaterial (43). Furthermore, recent studies suggest that for nanoparticles smaller

than 20 nm, surface area is not the only consideration as size-dependent properties and changes in physical and chemical reactivity and activity also become of importance (44, 45).

Animal studies have shown that engineered nanoparticles can elicit adverse pulmonary health effects, such as inflammation (46) and progressive pulmonary fibrosis (47). They have also identified that nanomaterials may elicit adverse cardiovascular effects, such as inflammation, blood platelet activation, plaque formation, and thrombosis (48, 49).

**3.1.3 Epidemiology** To date, there are no specific epidemiologic studies that link exposure to engineered nanomaterials with adverse health effects in the workplace. However, exposures to incidental ultrafine particles have been associated with adverse health outcomes in occupational settings. Acute respiratory distress syndrome triggered by exposure to metal nanoparticles was suspected as the cause of severe illness and death of several nickel smelters (50) and workers near a nickel arc spraying operation (51). Elevated nanoparticle concentrations have been associated with increased asthma symptoms (52) and airway inflammation (53). Adverse alterations in cardiac autonomic function have been associated with exposure to metals in welding fume (54).

Numerous environmental studies have associated exposure to incidental ultra-particles with adverse cardiopulmonary health outcomes that range from increased risk of hospital admission for heart attack (55), to changes in cardiac autonomic function (56), to increased prevalence of asthma (57, 58). These studies typically relate increases in the adverse health outcome to incremental changes in nanoparticle number concentration. For instance, Timonen et al. (56) identified a 13.5% decrease in low-to-high frequency of heart rate variability for each  $10^4 \text{ cm}^{-3}$  increase in the nanoparticle concentration. Increased cardiovascular mortality has been associated with living near a major road (59), where aerosols by number concentration are known to be dominated by nanoparticles (60).

## 3.2 Safety Hazards Fires and Explosions

A range of micron-sized materials produce dust clouds that present fire and explosion hazards in the workplace. Decreasing the size of a combustible material can reduce minimum ignition energy and increase combustion rate and also renders some noncombustible materials combustible (4). A standard apparatus and procedures can be used to characterize the explosive qualities of nanopowders used in the workplace as reviewed by Pritchard (61).

## 3.3 Regulation

There are no OELs specific to engineered nanomaterials at this time. As shown in Table 10.2, some nanomaterials are covered by composition-specific permissible exposure limits (PELs) established by the Occupational Safety and Health Administration (OSHA) (<http://www.osha.gov/SLTC/pel/index.html>). Others fall

**TABLE 10.2 Permissible Exposure Limits Applicable to Engineered Nanomaterials and Their Equivalent Particle Number and Surface Area Concentration Given Assumed Particle Sizes**

	PNOR <sup>a</sup>	Iron Oxide Fume <sup>b</sup>	Titanium Dioxide <sup>c</sup>	Silver Metal <sup>d</sup>
PEL (mg/m <sup>3</sup> )	5	10	15	0.01
<i>Assume Primary Particles of 20 nm Diameter</i>				
Number concentration (particle/cm <sup>3</sup> )	$1 \times 10^9$	$5 \times 10^8$	$8 \times 10^8$	230,000
Surface area concentration (μm <sup>2</sup> /cm <sup>3</sup> )	$1.5 \times 10^6$	$6 \times 10^5$	$1 \times 10^6$	286
<i>Assume Agglomerates 300 nm Diameter</i>				
Number concentration (particle/cm <sup>3</sup> )	350,000	150,000	250,000	70
Surface area concentration (μm <sup>2</sup> /cm <sup>3</sup> )	100,000	42,000	70,000	286

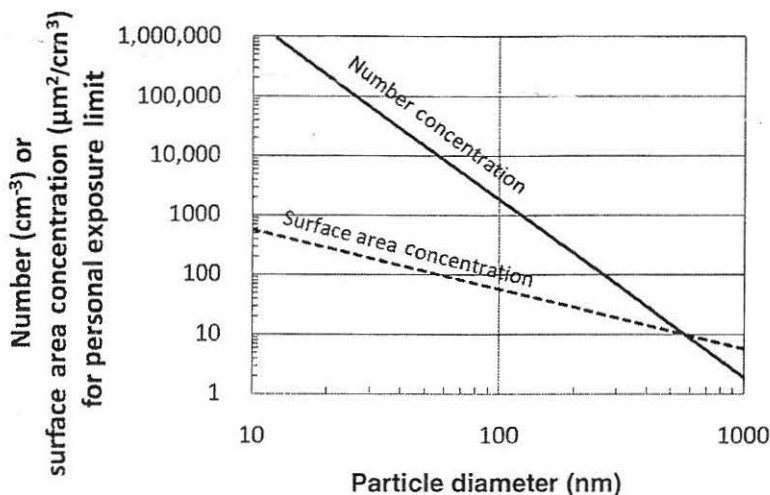
<sup>a</sup> Respirable; assumed unit density.<sup>b</sup> Respirable; assumed density = 4.8 g/cm<sup>3</sup>.<sup>c</sup> Total; assumed density = 4.3 g/cm<sup>3</sup>.<sup>d</sup> Respirable; assumed density = 10.5 g/cm<sup>3</sup>.

under the category of particles not otherwise regulated (PNOR) for which the PEL is 15 mg/m<sup>3</sup> for respirable and 5 mg/m<sup>3</sup> for total dust. PNOR applies to “biologically inert, insoluble, or poorly soluble particles” and is based on the ability of particles to overload the clearance mechanisms of the respiratory system simply by their physical presence, not their toxicity. OSHA regulations state that compliance with these standards is to be demonstrated by the facility via gravimetric sampling taken within the breathing zone of the worker. So from the OSHA perspective, mass concentrations are the only current consideration for particulate matter including nanoparticles.

PEL documentation is based on animal, human, and exposure data common to general industry. In most cases, there is considerable uncertainty whether composition-specific PELs are protective for nanomaterials. However, nanomaterials are designed to have unique properties that may well pose different health hazards than material found in general industry. Moreover, toxicity data suggest that at a minimum particle number or surface area concentration may be more relevant to the development of adverse health effects than mass concentration. As shown in Table 10.2 and depicted in Figure 10.8, the number and surface area concentrations required to attain a PEL mass concentration changes dramatically with the size of a particle. Although as noted before, even these metrics, number and surface area concentrations, do not take into account the size-dependent physicochemical properties of some nanomaterials that go beyond changes in surface area and particle number.

More recently, the NIOSH posted specific recommendations for workplaces where titanium dioxide (TiO<sub>2</sub>) is produced or used (62). These recommendations are based on toxicity data that show the tumorigenic effects of TiO<sub>2</sub> exposure are a function of particle size and surface area. These studies showed that nanosized TiO<sub>2</sub> particles with high surface area are associated with persistent inflammation substantially greater than that caused by larger particles. The recommend a time weighted average (TWA) exposure limit as 1.5 mg/m<sup>3</sup> for fine TiO<sub>2</sub> and 0.1 mg/m<sup>3</sup> for ultrafine TiO<sub>2</sub>.





**FIGURE 10.8** Number or surface area concentration required for a mass concentration equal to the PEL for silver metal (mass concentration in air of  $0.01 \text{ mg/m}^3$ ). Note these concentrations change dramatically for particles of different diameter.

Recent moves by the Environmental Protection Agency (EPA) to regulate engineered nanomaterials have relevance to occupational settings. In October 2008, the EPA formally published notice to manufacturers that it considers carbon nanotubes to be chemically different from conventional carbon compounds and therefore potentially subject to regulation through the “significant new use rule” (SNUR) under the Toxic Substances Control Act (TSCA) (63). This move means that companies and other entities that are currently manufacturing or importing nanomaterials must evaluate the implications of their activities under TSCA or risk enforcement action from the EPA. The EPA has also requested public comment on a petition filed to regulate nanoscale silver as a pesticide under the Federal Insecticide, Fungicide, and Rodenticide Act.

#### 4 INDUSTRIAL HYGIENE STRATEGY FOR ENGINEERED NANOMATERIALS

The sheer diversity of nanomaterials and the pace of new material development preclude a one-size-fits-all or a strictly measure-and-compare-to-the-OEL approach to EHS (64). Thus, the EHS professional is responsible to manage risk in an environment where no regulations exist and more often than not toxicity data are unavailable. A survey of EHS practices in the nanomaterials workplace shows great heterogeneity in the way companies deal with these hazard considerations (65). A more general strategy is needed to deal with the potential risks posed by engineered nanomaterials in the workplace. Here, we review some aspects of the anticipation, recognition, evaluation, and control of engineered nanomaterials. We then present how these activities central to the field of industrial hygiene can be applied within various overall risk frameworks to manage risk.



## 4.1 Anticipation and Recognition

**4.1.1 Processes** The way an engineered nanoparticle is produced, handled, or manipulated defines the size and concentration of particles that may be transported throughout the workplace either in the air or on surfaces. Generally, ingestion is a hazard with the potential to occur with any process and should be addressed with good worker hygiene. However, the type of and likelihood of inhalational and dermal hazards differs according to process and this must be taken into account in the development of safe practices.

**4.1.1.1 Production** Nanomaterials may be produced with top-down or bottom-up approaches. Top-down approaches involve the breakup of bulk materials into smaller materials. These approaches include mechanical processing, chemical processing, and etching. An example of mechanical processing is high-speed milling to grind together one or more solid material at low temperature. Wet milling may be done to promote chemical reaction at the same time as grind primary material. Chemical processing and etching typically involve potentially hazardous solvents and chemical precursors.

In contrast, bottom-up approaches to nanoparticle production involve the growth and self-assembly of single atoms and molecules. These approaches include liquid-phase techniques, where nanomaterials are crystallized or precipitated out of solution. For example, the sol-gel process is used commonly to produce ceramic nanomaterials by converting a liquid "sol" phase to a solid "gel" phase. Gas-phase nanoparticle synthesis involves the formation of particles by cooling a supersaturated vapor. The supersaturated vapor is usually formed by heating a solid until it evaporates into a background gas. Flame pyrolysis is the basis of production for many industrial metal-oxide nanomaterials, such as fumed silica, ultrafine titanium dioxide, and various forms of iron oxide. Other gas-phase synthesis methods include furnace flow reaction for metal nanoparticles, laser-induced pyrolysis for silicon-based nanomaterials, and plasma reaction for metal oxides (5).

Potential sources of exposure that may occur during the synthesis of nanomaterials have been discussed (5). Both gas-phase and liquid-phase synthetic methods can be used to generate nanomaterials. Although airborne particles may result from bursting bubbles or splashing, wet processes typically present dermal hazards. Inhalation exposure is unlikely during steps when nanomaterials are contained in liquids unless substantial bubbling and splashing occurs but may occur when nanomaterials are recovered and dried. Methods utilizing gas-phase precursors in the formulation of nanomaterials can result in airborne contamination of the workplace. In general, the exposure potential is thought to be low for production processes that are carried out in closed systems, which is often the case. However, exposures may occur if there are leaks in the system, during harvesting of nanomaterials, and/or maintaining and cleaning of system components. Dry dispersion of the nanomaterial or its precursors into the air is possible in mechanical processing steps.

**4.1.1.2 Handling** Many companies purchase nanomaterials for incorporation into their own products. Handling of the material (i.e., packaging, transfer, and cleaning

operations) may provide the greatest potential for airborne levels of nanomaterials and resultant occupational exposures (6). Exposures during handling are likely to be agglomerates of nanoparticles because the energy imparted to the nanomaterial are likely to be insufficient to break apart agglomerates (26, 66).

**4.1.1.3 Manipulation** During production, a part containing an engineered nanomaterial may require further manipulation. For example, epoxy composites that are reinforced with carbon nanotubes require sanding in the production of airplane wings. Gupta et al. (67) showed that sanding these composites released fragments of carbon nanotubes and particles with unique morphology (epoxy shards with carbon nanotubes projecting out of them). Exposure could also occur during product machining (e.g., cutting, drilling, and grinding), repair, destruction and recycling (4, 62).

**4.1.2 Workplaces** One can envision several generic types of workplaces where workers have a potential for occupational exposure to engineered nanomaterials, considering the different stages of a product that contains an engineered nanomaterial (Table 10.3). These workplaces can be subdivided into four groups: the research laboratory; the development facility; the production facility; the waste handling stream (6, 9). In the laboratory, typically a small number of researchers and technicians work to discover novel nanomaterials, while handling small quantities of materials with little data on toxicity. Possible exposure groups in this scenario include staff that maintains equipment and waste handlers in addition to the researchers and technicians themselves.

**TABLE 10.3    Possible Exposure Groups Defined by Workplace Setting**

Workplace Setting	Primary Tasks	Possible Exposure Groups
Research laboratory	Discover novel materials	Researchers
	Handle small quantities grams	Technicians
		Maintenance staff
		Waste handlers
Development facility	Ramp up production	<i>Above-mentioned groups plus</i>
	Develop new processes to incorporate material into products	Testing staff
	Optimize product for mass consumption	Transport staff
Production facility	Make, pack, ship, store product	<i>Above-mentioned groups plus</i>
	Transport product	Ancillary personnel
End-of-life waste and recycling facility		Direct user
	Disassembly of parts that contain nanomaterials	Personnel and staff involved in recycling

In the development facility, research and development staff work with technicians and testing staff to identify the processes, procedures, and products that will translate the novel discoveries made in the research laboratory into practical commercial endpoints. Often, these facilities house pilot-scale efforts intended to identify processes and procedures that substantially increase the output of a desirable nanomaterial. Work is performed to incorporate the nanomaterial into working prototype products and the products are tested to optimize performance. Although the quantity of material may be greater than in the research facility, there are usually less varied compounds in this type of environment. Often, the development step is when toxicity testing is done and can help inform industrial hygiene strategies. Exposure groups in the development facility include testing staff and transport staff in addition to those identified for the research laboratory.

The production facility houses processes and personnel required for mass production of a particular nanomaterial. These facilities may produce large quantities of certain types of nanomaterials as their final product and/or incorporate these materials into a final consumer product. All of the steps required to make, pack, ship, store, and transport the final product must be considered as potential sources of exposure. Thus, exposure groups for production facilities are specific to the type of processes on-going in the facility.

Waste handling and recycling centers are generally the endpoint for products that contain nanomaterials. A variety of handling procedures may be conducted that require worker interaction with nanomaterials. Using an automobile as an example (68), first fluids are removed that may contain nanomaterials such as the copper nanoparticles in some lubricants. Next, the vehicle is dismantled and most of the components are shredded. These components include windows that have nanosilver or nanoporous  $\text{SiO}_2$  layers, body parts that contain nanoclays, and tires that contain carbon black, silica nanofillers, and alumina nanofillers. The shredded components are separated into landfill or further processed to recover useful metals and nonmetals. Each step in the process offers opportunities for release of and exposure to nanomaterials.

## 4.2 Evaluation

**4.2.1 Monitoring** Workplace exposure monitoring is a key element to evaluating the risk of a hazard. This section focuses work that has been done to characterize the concentration of airborne particles. Although there are no consensus methods, a suite of techniques and instruments are available for assessing airborne exposures to engineered nanomaterials. These methods are far from ideal with numerous researchers actively seeking new ways to conveniently measure personal exposures.

**4.2.1.1 Instruments** There are different types of instruments and samplers available for use in assessing exposure to engineered nanomaterials. Instruments in this table are broken down by several attributes that include (i) instrument type (i.e., manual—time-integrated sample collected for subsequent analysis or direct-reading—real-time concentration provided to user directly); (ii) size resolution

(i.e., size-integrated—concentration integrated over many sizes or size-resolved—concentration provided in size bins); (iii) metric (i.e., number concentration, surface area concentration or mass concentration).

Time-integrated samples may be collected obtained with traditional size-selective samplers. Analysis of these samples by mass alone is likely to be inadequate to characterize exposures for engineered nanomaterials because the nanomaterial may in fact be obscured by other airborne particles present in the workplace atmosphere. However, chemical analysis of these filters may be conducted to determine the presence or absence of elements common to the nanomaterial (e.g., titanium for fumed silica). Differentiating between engineered nanomaterials and nanoparticles that are produced incidental to the production of the nanomaterial is very important if controls are to be put in place and if they are to be effective.

Electron microscopy of samples collected onto a filter can provide a more complete characterization of the airborne particles by size, morphology, and composition (see Fig. 10.3). A recent study by Peters et al. demonstrates this approach (11). Detailed data of these types are critical for selecting appropriate techniques for routine monitoring and control. They are also informative for the design of toxicity tests that are environmentally relevant, since it is increasingly clear that particle size, morphology, and composition (both bulk and surface), and concentration all affect the toxicity of nanomaterials. Although, computer automation is available to speed sample throughput and to collect data on many more particles, electron microscopy is inherently slow, costly, and lacking in standard methods for analyzing nanoparticles. Thus, at least in the short term, microscopy-based methods may be impractical routine assessments. However, additional studies of this type are essential to provide guidance for what may be needed for EHS compliance.

Several direct-reading instruments have found use in monitoring for engineered nanomaterials. Ultrafine and fine particles present in workplace atmospheres may be detected by number with the condensation particle counter (CPC) and by surface area with the diffusion charger. These instruments are unable to distinguish an engineered nanomaterial from any other airborne particle so the data obtained with them must be interpreted carefully. A detailed particle size distribution may be obtained with particle sizing instruments, such as the scanning mobility particle sizer and the aerodynamic particle sizer.

**4.2.1.2 Monitoring Strategies** It is useful to subdivide monitoring into three primary categories by intent: screening, extensive characterization, and routine monitoring. Screening involves the initial assessment of the workplace to determine evidence that the nanomaterial disperses into the workplace. Several researchers have used a CPC and an optical particle counter (OPC) as a relatively cost-effective means to screen a workplace for particle concentrations. Such measurements can be made throughout a facility to obtain spatial maps that help identify areas with elevated concentrations. They may also be used in a single position and their output correlated with activities associated with nanomaterial handling. Manually collected samples that are analyzed chemically are needed to determine the extent to which concentrations measured with the direct-reading instruments are actually engineered nanomaterial.



Extensive characterization involves the detailed measurement of airborne particle concentration by size, shape, and composition for the purpose of further evaluating the hazard posed by an engineered nanomaterial or to identify suitable routine monitoring methods. As already noted, it may be accomplished using electron microscopy of manually collected samples may be analyzed by computer-controlled scanning electron microscopy (SEM) or transmission electron microscopy (TEM) and/or with real-time measurements obtained with size-resolved instruments (e.g., scanning mobility particle sizer or aerodynamic particle sizer). Routine monitoring is performed to ensure that airborne concentrations stay below acceptable levels established by the facility. Routine monitoring involves collection of specific data, either from real-time monitors or time-integrated samplers, which allows the workplace concentration of engineered nanomaterials to be established.

**4.2.2 Medical Screening and Surveillance** Current guidelines from NIOSH suggest that scientific and medical evidence is insufficient to recommend specific medical screening of asymptomatic workers potentially exposed to engineered nanomaterials (69). They do, however, suggest that medical screening is appropriate for nanoparticles that are composed of a chemical or bulk material for which medical screening is currently recommended. Further recommendations include the use of established medical surveillance approaches to help assess whether control measures are effective and to identify new or unrecognized problems and health effects. The need to establish exposure registries for later epidemiologic study is stressed in the literature (70, 71).

## 4.3 Control

The traditional approach to the control of workplace hazards is well suited for application to engineered nanomaterials (9). This approach advises use of controls in the following hierarchy ordered from most to least favored: elimination, isolation, engineering, administrative, and lastly personal protection (72). If elimination or substitution of an engineered nanomaterial is impractical, the most effective form of control, as a general rule, is that applied nearest to the emission source. Thus, isolating the emission source from the general workplace environment combined with local exhaust ventilation is favored over the use of personal protective equipment, such as respirators, or the implementation of administrative controls. Here we consider each of these approaches for engineered nanomaterials.

**4.3.1 Elimination and Substitution** Typically, performance is the sole consideration in the selection or development of an engineered nanomaterial for incorporation into a product. In some cases, however, the EHS professional may have valuable input in this process that includes health and safety considerations (73). This may involve premarket testing to assess the possible health risks that might be associated with a given nanomaterial prior to going into full-scale production (9). Harper et al. envision an iterative testing process that combines product development with biological testing to develop benign nanoparticles using the principles of green chemistry (73). For

example, the biological activity of  $\text{TiO}_2$  nanomaterial may be reduced by altering its surface (43). Thus, the health hazard of this nanomaterial may conceivably be reduced by simply coating the nanomaterial with a second material that reduces biological activity but does not hamper performance (9, 43). Encapsulating a nanomaterial may also drastically reduce its likelihood of emission into a workplace and, hence, reduce exposures. These approaches have been used to reduce hazards in the handling of pesticides (74) and food products (75).

**4.3.2 Isolation** In the short term, isolation is perhaps the single most effective and easy-to-implement control for engineered nanomaterials. Isolation is the removal of the source of the hazardous exposure from the worker's environment (65, 72). It may be achieved by placing a process that involves an engineered nanomaterial in an enclosure with physical barriers or in an area where workers are unlikely to come in contact with the process. Isolation is often most effective when implemented during initial design of facilities, although retrofitting existing processes is possible. However, exposure may result despite isolation for airborne hazards and during maintenance activities (9).

**4.3.3 Engineering Controls** Like any airborne particle hazard, exposure to engineered nanomaterials can be reduced with engineering controls, which include general (dilution) or local exhaust ventilation (76). The successful design of ventilation systems relies heavily on the airborne behavior of the contaminant. This behavior for engineered nanomaterials depends on particle size, shape, and density. Airborne nanomaterials that are fit the definition of fine or ultrafine mode aerosol (i.e., submicrometer, fairly spherical, near unit density) will follow airflow streamlines at velocities typical of a workplace and within hoods of ventilation ducts. These particles may be treated as fine particles for capture and transfer in local exhaust ventilation calculations (76, 77). Greater consideration must be given to large ( $>1\ \mu\text{m}$ ) dense (material density  $>1\ \text{g/cm}^3$ ) airborne particles with engineered nanostructure that have been observed in the workplace (Fig. 10.3a–d) (11). The inertia of these type of particles require greater attention to air capture velocity to ensure their collection by a ventilation hood but these principles are not unique to nanomaterials and are covered thoroughly in ventilation manuals (76).

A common practice is to handle powders in a laboratory hood, which is part of a local exhaust ventilation system (77). Control in a hood may be incomplete due to recirculating airflow patterns that surround a worker (78). Thus, caution should be exercised for the handling of highly toxic materials, including engineered nanomaterials. Mobile local exhaust ventilation systems are available for nonroutine operations or where costs prohibit installation of a complete stationary system (79). Methner (79) identified that use of a mobile local exhaust ventilation system combined with targeted changes in work practice dramatically reduced airborne emissions (greater than 78% reduction in air concentration by number) during cleanout of a reactor used to produce metal-based engineered nanomaterials to be used as catalysts.



General exhaust ventilation is applicable for contaminants that are not highly toxic because the nanomaterial will not be removed from the environment but instead diluted. Pui et al. demonstrate that relatively inexpensive filters in recirculating air systems can substantially reduce the concentration of truly nanosized particles in a room (80). They present a numerical model to estimate particle number concentration as a function of time after turning a recirculation system on,  $N(t)$ , as

$$N(t) = ae^{bt} + c$$

where  $a = N_0 - c$ ,  $b = -(Q/V)/\eta$ ,  $c = I/(VQ\eta)$ ,  $N_0$  is the initial number concentration in the room,  $Q$  is the ventilation flow rate,  $V$  is the room volume,  $\eta$  is the average one-pass particle removal efficiency, and  $I$  is the infiltration rate of material entering the room divided by the room volume and has units of particles  $\text{length}^{-3} \text{time}^{-1}$ . Although this equation assumes a uniform distribution of particles within a room, which may be poor for nanosized particles, it does allow a framework for evaluating recirculation.

**4.3.4 Administrative Controls** Administrative control involves implementation of practices that reduce workplace exposures to a hazard. These practices include increased management involvement, training of employees, and rotation of employees. An example from a nanotechnology laboratory from Schulte et al. is the strict practice of maintaining clean room conditions (9). Employee rotation has been applied to reduce ergonomic stressors but it must be balanced with the fact that more workers will be exposed to a hazard.

**4.3.5 Personal Protective Equipment** Personal protective equipment (PPE), such as the use of respirators to control inhalation exposure, is the last form of control recommended in the traditional industrial hygiene control hierarchy. This de-emphasis on PPE stems from the fact that PPE are often uncomfortable, interfere with communication and vision, and are effective only when properly used. They should be used only when other methods are not feasible, and they require a well-managed, complete, and systematic program as per OSHA guidelines (81).

Substantial research has been conducted on the effectiveness of respirators as protection against inhalation hazards. Most respirators rely on fibers for collection of particulate, and their effectiveness depends on the extent to which particles deviate from an airflow streamline due to diffusion, interception, impaction, and sedimentation. Similar to particle deposition in the respiratory system (Fig. 10.7), the overall collection efficiency of a fiber-based respirator exhibits a characteristic dip where diffusion and impaction are least effective at causing a particle to deviate and hit a fiber (20). Rengasamy et al. found that the penetration of nanosized particles through N95 and P100 respirators follow filtration theory in that penetration increases as particle size decreases (82). They identified that the most penetrating particle size was in the range of 30–40 nm and that the performance meets the respirator ratings as indicated by their N95 and P100 labeling.

#### 4.4 Overall Risk Management

A risk management strategy combines the activities of anticipation, recognition, evaluation, and control into a coherent plan to reduce the likelihood that a worker will develop an adverse health outcome as a result of a workplace exposure. Several strategies have been recommended for managing risk in the workplace where engineered nanomaterials are found present. For assessing risk of engineered nanomaterials, the general risk management paradigm is still valid although there are tremendous uncertainties at the present time. In the absence of specific guidelines, NIOSH recommends interim precautionary measures be developed and implemented where engineered nanomaterials enter the workplace (4). They suggest using a hazards-based approach to evaluate exposures and for developing precautionary measures as are consistent with good occupational safety and health practices.

Control banding has been proposed for addressing engineered nanomaterial hazards. Control banding provides a framework for making decisions on the appropriateness of different control options in the absence of complete information, which makes it particularly amenable to control of engineered nanomaterials (83–85). Paik et al. (84) present a control banding tool specifically developed for working with engineered nanomaterials and then apply this tool to evaluate the hazards associated with five processes that involve engineered nanomaterials in two Department of Energy research laboratories. A severity score from 0 to 100 is assigned to a nanomaterial based on what is known about surface chemistry, shape, diameter, solubility, carcinogenicity, and toxicity. A probability score from 0 to 100 is given to reflect the ability of the nanomaterial to become an exposure hazard. Probability is based on quantity used, dustiness/mistiness, number of employees with similar exposures, frequency of operation, and duration of operation. A risk level is assigned that is a combination of probability and severity with appropriate recommended actions that range from use of general ventilation to seek specialist advice.

Kandlikar et al. advise the use of expert judgment to address the considerable uncertainties when assessing health risks posed by engineered nanomaterials in the workplace (86). In this approach, expert opinion is used to help judge unknowns such as severity or probability in the control banding approach mentioned above. They suggest that measurements should be made where uncertainty among experts is greatest.

Others have taken a physiological approach to addressing nanomaterial hazard evaluation. Liao et al. (87) used a physiological-based model to estimate the burden of  $\text{TiO}_2$  expressed as surface area in alveolar space and the interstitium based on exposure data. They then estimated the lung cancer risk by combining burden estimates with dose–response data from animal exposures.

### 5 FUTURE OUTLOOK

In the near future, the pace with which new engineered nanomaterials are developed is expected to increase. This increase will introduce not only new materials but also new processes and work practices into the workplace. EHS programs must accommodate

for these changes in the workplace to ensure worker protections. We expect that a continuation in the growth in EHS resources available for the practitioner and researcher. These resources should clarify some of the key questions in how to manage risk in the face of new nanomaterials. These questions include how nanomaterials are classified; what exposure metric is best suited for monitoring; what levels are acceptable for different materials; and what the limits of controls are. In the longer term, we should see engineered nanomaterials be used to substantially enhance the ability to conduct EHS. For example, great promise is held for use of nanomaterials in detection of gases and may translate into particulate detection as well.

## ACKNOWLEDGMENTS

The authors would like to acknowledge graduate students who have been involved in some of the work discussed here. In particular, Sherrie Elzey, Heaweon Park, and Ronald Johnson. This material is based upon work partially supported by Grant No. 1R01OH009448-01(VHG) and Grant No. K01OH009255-01 (TMP) from CDC-NIOSH. Its contents are solely the responsibility of the authors and do not necessarily represent the official views of NIOSH.

## BIBLIOGRAPHY

1. B. Park, K. Donaldson, R. Duffin, L. Tran, F. Kelly, I. Mudway, J. P. Morin, R. Guest, P. Jenkinson, Z. Samaras, M. Giannouli, H. Kouridis, P. Martin, "Hazard and Risk Assessment of a Nanoparticulate Cerium Oxide-Based Diesel Fuel Additive: A Case Study," *Inhal. Toxicol.* **20**(6), 547–566 (2008).
2. V. K. Sharma, R. A. Yngard, Y. Lin, "Silver Nanoparticles: Green Synthesis and Their Antimicrobial Activities," *Adv. Colloid. Interface Sci.* **145**(1–2), 83–96 (2009).
3. ISO, *Workplace Atmospheres—Ultrafine, Nanoparticle, and Nano-Structured Aerosols—Exposure Characterization and Assessment*, 2007, ISO/TR 27628:2007(E): Geneva, Switzerland.
4. NIOSH, Approaches to Safe Nanotechnology. <http://www.cdc.gov/niosh/topics/nanotech/safenano/>, 2006.
5. R. J. Aitken, K. S. Creeley, C. L. Tran, *Nanoparticles: An Occupational Hygiene Review*, Health and Safety Executive, Edinburgh, 2000.
6. EPA, *Nanotechnology White Paper*, U.S. Environmental Protection Agency, Washington, DC, 2007.
7. T. Papp, D. Schiffmann, D. Weiss, V. Castranova, V. Vallyathan, Q. Rahman, "Human Health Implications of Nanomaterial Exposure," *Nanotoxicology* **2**(1), 9–27 (2008).
8. G. Oberdorster, E. Oberdorster, J. Oberdorster, "Nanotoxicology: An Emerging Discipline Evolving from Studies of Ultrafine Particles," *Environ. Health Perspect.* **113**(7), 823–839 (2005).
9. P. Schulte, C. Geraci, R. Zumwalde, M. Hoover, E. Kuempel, "Occupational Risk Management of Engineered Nanoparticles," *J. Occup. Environ. Hyg.* **5**(4), 239–249 (2008).

10. ASTM, *Terminology for Nanotechnology*, ASTM E2456-06, Available at [www.astm.org](http://www.astm.org), 2006.
11. T. M. Peters, S. Elzey, R. Johnson, H. Park, V. H. Grassian, T. Maher, P. O'Shaughnessy, "Airborne Monitoring to Distinguish Engineered Nanomaterials from Incidental Particles for Environmental Health and Safety," *J. Occup. Environ. Hyg.* **6**(2), 73–81 (2009).
12. A. J. Haes, C. L. Haynes, A. D. McFarland, G. C. Schatz, R. P. Van Duyne, S. Zou, "Plasmonic Materials for Surface Enhanced Sensing and Spectroscopy," *MRS Bull.* **30**(5), 368–375 (2005).
13. A. P. Tinke, R. Govoreanu, K. Vanhoutte, "Particle Size and Shape Characterization of Nano and Submicron Liquid Dispersions," *Am. Pharm. Rev.* **9**(6), 1 (2006).
14. V. H. Grassian, "When Size Really Matters: Size-Dependent Properties and Surface Chemistry of Metal and Metal Oxide Nanoparticles in Gas and Liquid Phase Environments," *J. Phys. Chem. C* **112**(47), 18303–18313 (2008).
15. S. Elzey, R. G. Larsen, C. Howe, and V. H. Grassian, "Nanoscience and Nanotechnology: Environmental and Health Impacts," in K. J. Klabunde and R. M. Richards, Eds., *Nanoscale Materials in Chemistry*, 2nd ed., John Wiley & Sons, Hoboken, NJ, 2009.
16. H. Fairbrother, B. Smith, J. Wnuk, K. Wepasnick, W. P. Ball, H. Cho, and F. K. Bangash, "Surface Oxides on Carbon Nanotubes (CNTs): Effects on CNT Stability and Sorption Properties in Aquatic Environments," in V. H. Grassian, Ed., *Nanoscience and Nanotechnology: Environmental and Health Impacts*, John Wiley & Sons, Hoboken, NJ, 2008.
17. J. L. Nadeau, J. H. Priester, G. D. Stucky, and P. A. Holden, "Bacterial Interactions with CdSe Quantum Dots and Environmental Implications," in V. H. Grassian, Ed., *Nanoscience and Nanotechnology: Environmental and Health Impacts*, John Wiley & Sons Inc., 2008, pp. 197–221.
18. K. Sellers, C. Mackay, L. L. Bergeson, S. R. Clough, M. Hoyt, J. Chen, K. Henry, J. Hamblen, *Nanotechnology and the Environment*, CRC Press, Boca Raton, 2009. p. 281.
19. ICRP, *Human Respiratory Tract Model for Radiological Protection*, Publication 66, Pergamon Press, Oxford, UK. *Ann. ICRP* **24**, 272 (1994).
20. W. C. Hinds, *Aerosol Technology: Properties, Behavior, and Measurement of Airborne Particles*, 2nd ed., John Wiley & Sons, Inc., New York, 1999, p. 483.
21. C. Kleinstreuer, Z. Zhang, J. F. Donohue, "Targeted Drug-Aerosol Delivery in the Human Respiratory System," *Ann. Rev. Biomed. Eng.* **10**, 195–220 (2008).
22. J. Londahl, A. Massling, J. Pagels, E. Swietlicki, E. Vaclavik, S. Loft, "Size-Resolved Respiratory-Tract Deposition of Fine and Ultrafine Hydrophobic and Hygroscopic Aerosol Particles During Rest and Exercise," *Inhal. Toxicol.* **19**(2), 109–116 (2007).
23. B. Asgharian, O. T. Price, "Deposition of Ultrafine (NANO) Particles in the Human Lung," *Inhal. Toxicol.* **19**(13), 1045–1054 (2007).
24. Y. Zhou, W. C. Su, Y. S. Cheng, "Fiber Deposition in the Tracheobronchial Region: Deposition Equations," *Inhal. Toxicol.* **20**(13), 1191–1198 (2008).
25. A. D. Maynard, P. A. Baron, M. Foley, A. A. Shvedova, E. R. Kisin, V. Castranova, "Exposure to Carbon Nanotube Material: Aerosol Release During the Handling of Unrefined Single-Walled Carbon Nanotube Material," *J. Toxicol. Environ. Health A* **67** (1), 87–107 (2004).
26. M. M. Methner, M. E. Birch, D. E. Evans, B. K. Ku, K. Crouch, M. D. Hoover, "Identification and Characterization of Potential Sources of Worker Exposure to

- Carbon Nanofibers During Polymer Composite Laboratory Operations," *J. Occup. Environ. Hyg.* **4**(12), D125–D130 (2007).
27. M. Semmler-Behnke, S. Takenaka, S. Fertsch, A. Wenk, J. Seitz, P. Mayer, G. Oberdorster, W. G. Kreyling, "Efficient Elimination of Inhaled Nanoparticles from the Alveolar Region: Evidence for Interstitial Uptake and Subsequent Reentrainment onto Airways Epithelium," *Environ. Health Perspect.* **115**(5), 728–733 (2007).
  28. R. R. Mercer, J. Scabilloni, L. Wang, E. Kisin, A. R. Murray, D. Schwegler-Berry, A. A. Shvedova, V. Castranova, "Alteration of Deposition Pattern and Pulmonary Response as a Result of Improved Dispersion of Aspirated Single-Walled Carbon Nanotubes in a Mouse Model," *Am. J. Physiol. Lung. Cell. Mol. Physiol.* **294**(1), L87–L97 (2008).
  29. G. Oberdörster, Z. Sharp, V. Atudorei, A. Elder, R. Gelein, W. Kreyling, C. Cox, "Translocation of Inhaled Ultrafine Particles to the Brain," *Inhal. Toxicol.* **16**(6–7), 437–445 (2004).
  30. G. Oberdörster, Z. Sharp, V. Atudorei, A. Elder, R. Gelein, A. Lunts, W. Kreyling, C. Cox, "Extrapulmonary Translocation of Ultrafine Carbon Particles Following Whole-Body Inhalation Exposure of Rats," *J. Toxicol. Environ. Health A* **65**(20), 1531–1543 (2002).
  31. A. Elder, R. Gelein, V. Silva, T. Feikert, L. Opanashuk, J. Carter, R. Potter, A. Maynard, J. Finkelstein, G. Oberdorster, "Translocation of Inhaled Ultrafine Manganese Oxide Particles to the Central Nervous System," *Environ. Health Perspect.* **114**(8), 1172–1178 (2006).
  32. A. Elder, G. Oberdorster, "Translocation and Effects of Ultrafine Particles Outside of the Lung," *Clin. Occup. Environ. Med.* **5**(4), 785–796 (2006).
  33. W. Moller, K. Felten, K. Sommerer, G. Scheuch, G. Meyer, P. Meyer, K. Haussinger, W. G. Kreyling, "Deposition, Retention, and Translocation of Ultrafine Particles from the Central Airways and Lung Periphery," *Am. J. Res. Crit. Care Med.* **177**(4), 426–432 (2008).
  34. S. S. Tinkle, J. M. Antonini, B. A. Rich, J. R. Roberts, R. Salmen, K. DePree, E. J. Adkins, "Skin as a Route of Exposure and Sensitization in Chronic Beryllium Disease," *Environ. Health Perspect.* **111**(9), 1202–1208 (2003).
  35. L. J. Mortensen, G. Oberdorster, A. P. Pentland, L. A. DeLouise, "In Vivo Skin Penetration of Quantum Dot Nanoparticles in the Murine Model: The effect of UVR," *Nano Lett.* **8**(9), 2779–2787 (2008).
  36. L. W. Zhang, N. A. Monteiro-Riviere, "Assessment of Quantum Dot Penetration into Intact, Tape-Stripped, Abraded and Flexed Rat Skin," *Skin Pharmacol. Physiol.* **21**(3), 166–180 (2008).
  37. P. H. Hoet, I. Bruske-Hohlfeld, O. V. Salata, "Nanoparticles: Known and Unknown Health Risks," *J. Nanobiotechnol.* **2**(12), (2004).
  38. G. Oberdörster, J. Ferin, B. E. Lenhert, "Correlation Between Particle Size, In Vivo Particle Persistence, and Lung Injury," *Environ. Health Perspect.* **105** (Suppl 5), 173–179 (1994).
  39. R. Duffin, L. Tran, D. Brown, V. Stone, K. Donaldson, "Proinflammogenic Effects of Low-Toxicity and Metal Nanoparticles In Vivo and In Vitro: Highlighting the Role of Particle Surface Area and Surface Reactivity," *Inhal. Toxicol.* **19**(10), 849–856 (2007).
  40. C. Monteiller, L. Tran, W. MacNee, S. Faux, A. Jones, B. Miller, K. Donaldson, "The Pro-Inflammatory Effects of Low-Toxicity Low-Solubility Particles, Nanoparticles and Fine Particles, on Epithelial Cells In Vitro: the Role of Surface Area," *Occup. Environ. Med.* **64**(9), 609–615 (2007).



41. D. Hohr, Y. Steinfartz, R. P. Schins, A. M. Knaapen, G. Martra, B. Fubini, P. J. Borm, "The Surface Area Rather Than the Surface Coating Determines the Acute Inflammatory Response After Instillation of Fine and Ultrafine TiO<sub>2</sub> in the Rat," *Int. J. Hyg. Environ. Health* **205**(3), 239–244 (2002).
42. T. Stoeger, C. Reinhard, S. Takenaka, A. Schroeppel, E. Karg, B. Ritter, J. Heyder, H. Schulz, "Instillation of Six Different Ultrafine Carbon Particles Indicates a Surface Area Threshold Dose for Acute Lung Inflammation in Mice," *Environ. Health Perspect.* **114**(3), 328–333 (2006).
43. D. B. Warheit, C. M. Sayes, K. L. Reed, K. A. Swain, "Health Effects Related to Nanoparticle Exposures: Environmental, Health and Safety Considerations for Assessing Hazards and Risks," *Pharmacol. Ther.* **120**(1), 35–42 (2008).
44. V. H. Grassian, A. Adamcakova-Dodd, J. M. Pettibone, P. T. O'Shaughnessy, P. S. Thorne, "Inflammatory Response of Mice to Manufactured Titanium Dioxide Nanoparticles: Comparison of Size Effects Through Different Exposure Routes," *Nanotoxicology* **1**, 211–226 (2007).
45. J. Jiang, G. Oberdorester, A. Elder, R. Gelein, P. Mercer, P. Biswas, "Does Nanoparticle Activity Depend Upon Size and Crystal Phase?," *Nanotoxicology* **2**, 33 (2008).
46. C. W. Lam, J. T. James, R. McCluskey, S. Arepalli, R. L. Hunter, "A Review of Carbon Nanotube Toxicity and Assessment of Potential Occupational and Environmental Health Risks," *Crit Rev Toxicol* **36**(3), 189–217 (2006).
47. A. A. Shvedova, E. R. Kisin, R. Mercer, A. R. Murray, V. J. Johnson, A. I. Potapovich, Y. Y. Tyurina, O. Gorelik, S. Arepalli, D. Schwegler-Berry, A. F. Hubbs, J. Antonini, D. E. Evans, B. K. Ku, D. Ramsey, A. Maynard, V. E. Kagan, V. Castranova, P. Baron, "Unusual Inflammatory and Fibrogenic Pulmonary Responses to Single-Walled Carbon Nanotubes in Mice," *Am. J. Physiol. Lung Cell Mol. Physiol.* **289**(5), L698–L708 (2005).
48. E. Oesterling, N. Chopra, V. Gavalas, X. Arzuaga, E. J. Lim, R. Sultana, D. A. Butterfield, L. Bachas, B. Hennig, "Alumina nanoparticles induce expression of endothelial cell adhesion molecules," *Toxicol. Lett.* **178**(3), 160–166 (2008).
49. A. Gojova, B. Guo, R. S. Kota, J. C. Rutledge, I. M. Kennedy, A. I. Barakat, "Induction of Inflammation in Vascular Endothelial Cells by Metal Oxide Nanoparticles: Effect of Particle Composition," *Environ. Health Perspect.* **115**(3), 403–409 (2007).
50. A. I. M. Sandstrom, S. G. I. Wall, A. Taube, "Cancer Incidence and Mortality Among Swedish Smelter Workers," *Br. J. Ind. Med.* **46**, 82–89 (1989).
51. R. E. G. Rendall, J. I. Phillips, K. A. Renton, "Death Following Exposure to Fine Particulate Nickel from a metal arc process," *Ann. Occup. Hyg.* **38**, 921–930 (1994).
52. H. Wichmann, A. Peters, "Epidemiological Evidence of the Effects of Ultrafine Particles Exposure," *Trans. Roy. Soc. Lond. A* **358**, 2751–2769 (2000).
53. K. Donaldson, V. Stone, P. S. Gilmour, D. M. Brown, W. MacNee, "Ultrafine Particles: Mechanisms of Lung Injury," *Philos. Trans. R. Soc. Lond. A* **358**, 2741–2749 (2000).
54. S. R. Magari, J. Schwartz, P. L. Williams, R. Hauser, T. J. Smith, D. C. Christiani, "The Association Between Personal Measurements of Environmental Exposure to Particulates and Heart Rate Variability," *Epidemiology* **13**(3), 305–310 (2002).
55. S. von Klot, A. Peters, P. Aalto, T. Bellander, N. Berglind, D. D'Ippoliti, R. Elosua, A. Hormann, M. Kulmala, T. Lanki, H. Lowe, J. Pekkanen, S. Picciotto, J. Sunyer, F.



- Forastiere, "Ambient Air Pollution is Associated with Increased Risk of Hospital Cardiac Readmissions of Myocardial Infarction Survivors in Five European Cities," *Circulation* **112**(20), 3073–3079 (2005).
56. K. L. Timonen, E. Vanninen, J. De Hartog, A. Ibaldo-Mulli, B. Brunekreef, D. R. Gold, J. Heinrich, G. Hoek, T. Lanki, A. Peters, T. Tarkiainen, P. Tiittanen, W. Kreyling, J. Pekkanen, "Effects of Ultrafine and Fine Particulate and Gaseous Air Pollution on Cardiac Autonomic Control in Subjects with Coronary Artery Disease: The ULTRA Study," *J. Expo. Sci. Environ. Epidemiol.* **16**(4), 332–341 (2006).
  57. R. J. Delfino, P. J. E. Quintana, J. Floro, V. M. Gastanaga, B. S. Samimi, M. T. Kleinman, L. J. S. Liu, C. Bufalino, C. F. Wu, C. E. McLaren, "Association of FEV1 in Asthmatic Children with Personal and Microenvironmental Exposure to Airborne Particulate Matter," *Environ. Health Perspect.* **112**(8), 932 (2004).
  58. J. S. Lwebuga-Mukasa, T. J. Oyana, C. Johnson, "Local Ecological Factors, Ultrafine Particulate Concentrations, and Asthma Prevalence Rates in Buffalo, New York, Neighborhoods," *J. Asthma* **42**(5), 337–348 (2005).
  59. G. Hoek, B. Brunekreef, S. Goldbohm, P. Fischer, P. A. van den Brandt, "Association Between Mortality and Indicators of Traffic-Related Air Pollution in the Netherlands: A Cohort Study," *Lancet* **360**(9341), 1203–1209 (2002).
  60. Y. Zhu, W. C. Hinds, S. Kim, C. Sioutas, "Concentration and Size Distribution of Ultrafine Particles Near a Major Highway," *J. Air Waste Manag. Assoc.* **52**(9), 1032–1042 (2002).
  61. D. K. Prichard, *Literature Review: Explosion Hazards Associated with Nanopowders*, Health & Safety Laboratory, Buxton, UK, 2004, p. 17.
  62. NIOSH, *Current Intelligence Bulletin: Evaluation of Health Hazard and Recommendations for Occupational Exposure to Titanium Dioxide*, NIOSH Docket No. 100. Available at <http://www.cdc.gov/niosh/review/public/tio2/pdfs/TIO2Draft.pdf>. 2005. (Note: Web site provides docket that will be updated recommendations and public comment [www.cdc.gov/niosh/docket/NIOSHdocket0033.html](http://www.cdc.gov/niosh/docket/NIOSHdocket0033.html)).
  63. EPA, *Toxic Substances Control Act Inventory Status of Carbon Nanotubes*, in Federal Register, 2008.
  64. A. D. Maynard, "Nanotechnology: The Next Big Thing, or Much Ado About Nothing?," *Ann. Occup. Hyg.* **51**(1), 1–12 (2007).
  65. J. A. Conti, K. Killpack, G. Gerritzen, L. Huang, M. Mircheva, M. Delmas, B. H. Harthorn, R. P. Appelbaum, P. A. Holden, "Health and Safety Practices in the Nanomaterials Workplace: Results from an International Survey," *Environ. Sci. Technol.* **42**(9), 3155–3162 (2008).
  66. C. J. Tsai, C. H. Wu, M. L. Leu, S. C. Chen, C. Y. Huang, P. J. Tsai, F. H. Ko, "Dustiness Test of Nanopowders Using a Standard Rotating Drum with a Modified Sampling Train," *J. Nanopart. Res.* **11**, 121–131 (2009).
  67. A. Gupta, M. L. Clark, D. J. Gaspar, M. G. Yost, G. M. Gross, P. E. Rempes, and J. C. Martin, "Evaluating the Potential for Release of Carbon Nanotubes and Subsequent Occupational Exposure During Processing of a Nanocomposite," in American Association for Aerosol Research, Reno, NV, 2007.
  68. K. Ostertag, B. Husing, "Identification of Starting Points for Exposure Assessment in the Post-Use Phase of Nanomaterial-Containing Products," *J. Cleaner Prod.* **16**(8–9), 938–948 (2008).

69. NIOSH, *Interim Guidance for the Medical Screening of Workers Potentially Exposed to Engineered Nanoparticles*, NIOSH Docket No. 115, 2007, Available at <http://www.cdc.gov/niosh/review/public/115/>.
70. P. A. Schulte, D. Trout, R. D. Zumwalde, E. Kuempel, C. L. Geraci, V. Castranova, D. J. Mundt, K. A. Mundt, W. E. Halperin, "Options for Occupational Health Surveillance of Workers Potentially Exposed to Engineered Nanoparticles: State of the Science," *J. Occup. Environ. Med.* **50**(5), 517–526 (2008).
71. M. Nasterlack, A. Zober, C. Oberlinner, "Considerations on Occupational Medical Surveillance in Employees Handling Nanoparticles," *Int. Arch. Occup. Environ. Health* **81**(6), 721–726 (2008).
72. D. J. Burton, "General Methods for the Control of Airborne Hazards," in S. R. DiNardi, Ed., *The Occupational Environment: Its Evaluation, Control, and Management*, AIHA Press, Fairfax, VA, 2003.
73. S. L. Harper, J. A. Dahl, B. L. S. Maddux, R. L. Tanguay, J. E. Hutchison, "Proactively Designing Nanomaterials to Enhance Performance and Minimise Hazard," *Int. J. Nanotechnol.* **5**(1), 124–142 (2008).
74. M. Maroni, A. Fait, C. Colosio, "Risk Assessment and Management of Occupational Exposure to Pesticides," *Toxicol. Lett.* **107**(1–3), 145–153 (1999).
75. C. Onwulata, *Encapsulated and Powdered Foods*, CRC Press, Boca Raton, 2005.
76. D. K. George, S. R. DiNardi, and R. G. Handy, "An Introduction to the Design of Local Exhaust Ventilation Systems," in S. R. DiNardi, Ed., *The Occupational Environment: Its Evaluation, Control, and Management*, AIHA Press, Fairfax, VA, 2003.
77. K. Heinonen, I. Kulmala, A. Saamanen, "Local Ventilation for Powder Handling: Combination of Local Supply and Exhaust Air," *Am. Ind. Hyg. Assoc. J.* **57**(4), 356–364 (1996).
78. M. R. Flynn, E. D. Sills, "Numerical Simulation of Human Exposure to Aerosols Generated During Compressed Air Spray-Painting in Cross-Flow Ventilation Booths," *Trans. ASME* **123**, 64–70 (2001).
79. M. M. Methner, "Engineering Case Reports. Effectiveness of Local Exhaust Ventilation (LEV) in Controlling Engineered Nanomaterial Emissions During Reactor Cleanout Operations," *J. Occup. Environ. Hyg.* **5**(6), D63–D69 (2008).
80. D. Y. H. Pui, C. Qi, N. Stanley, G. Oberdorster, A. Maynard, "Recirculating Air Filtration Significantly Reduces Exposure to Airborne Nanoparticles," *Environ. Health Perspect.* **116**(7), 863–866 (2008).
81. C. E. Colton and T. J. Nelson, "Respiratory Protection," in S. R. DiNardi, Ed., *The Occupational Environment: Its Evaluation, Control, and Management*, AIHA Press, Fairfax, VA, 2003.
82. S. Rengasamy, W. P. King, B. C. Eimer, R. E. Shaffer, "Filtration Performance of NIOSH-Approved N95 and P100 Filtering Facepiece Respirators Against 4 to 30 Nanometer-Size Nanoparticles," *J. Occup. Environ. Hyg.* **5**(9), 556–564 (2008).
83. C. D. Money, "European Experiences in the Development of Approaches for the Successful Control of Workplace Health Risks," *Ann. Occup. Hyg.* **47**(7), 533–540 (2003).
84. S. Y. Paik, D. M. Zalk, P. Swuste, "Application of a Pilot Control Banding Tool for Risk Level Assessment and Control of Nanoparticle Exposures," *Ann. Occup. Hyg.* **52**(6), 419–428 (2008).

85. D. M. Zalk, D. I. Nelson, "History and Evolution of Control Banding: A Review," *J. Occup. Environ. Hyg.* **5**(5), 330–346 (2008).
86. M. Kandlikar, G. Ramachandran, A. Maynard, B. Murdock, W. A. Toscano, "Health Risk Assessment for Nanoparticles: A Case for Using Expert Judgment," *J. Nanopart. Res.* **9**(1), 137–156 (2007).
87. C. M. Liao, Y. H. Chiang, C. P. Chio, "Model-Based Assessment for Human Inhalation Exposure Risk to Airborne Nano/Fine Titanium Dioxide Particles," *Sci. Total Environ.* **407**(1), 165–677 (2008).

# PATTY'S INDUSTRIAL HYGIENE

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Sixth Edition

Volume 1

HAZARD RECOGNITION

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Published by John Wiley & Sons, Inc., Hoboken, New Jersey

Published simultaneously in Canada

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***Library of Congress Cataloging-in-Publication Data:***

Patty's industrial hygiene. – 6th ed. / edited by Vernon E. Rose, Barbara Cohnssen.

p. cm.

Includes index.

ISBN 978-0-470-07488-6 (cloth : set) — ISBN 978-0-470-07484-8 (v. 1) — ISBN 978-0-470-07485-5 (v. 2) — ISBN 978-0-470-07486-2 (v. 3) — ISBN 978-0-470-07487-9 (v. 4)

I. Industrial hygiene—Case studies. I. Rose, Vernon E. II. Cohnssen, Barbara.

III. Patty, F. A. (Frank Arthur), 1897- Industrial hygiene and toxicology.

IV. Title: Industrial hygiene. RC967.P37 2011 613.6'2—dc22

2010011931

Printed in the United States of America

10 9 8 7 6 5 4 3 2 1