

# Potential risks of nanomaterials and how to safely handle materials of uncertain toxicity

In the last few years, the number of research studies on the toxicity of different types of nanomaterials has increased dramatically. These studies have suggested effects at the cellular level and in short-term animal tests. The effects seen depend on the base material of the nanoparticle, its size and structure, and its substituents and coatings. Additional toxicology testing is being funded or planned by the National Nanotechnology Infrastructure Network and other research organizations in the US and in Europe. Nanomaterials of uncertain toxicity can be handled using the same precautions currently used at universities to handle other materials of unknown toxicity: use of exhaust ventilation (such as fume hoods and vented enclosures) to prevent inhalation exposure during procedures that may release aerosols or fibers and use of gloves to prevent dermal exposure. This article presents an overview of some of the major questions in nanotoxicology and also discusses the best practices that universities such as MIT and others are currently using to prevent exposure.

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## WHAT ARE NANOMATERIALS?

The focus of this article is engineered nanoparticles that are intentionally

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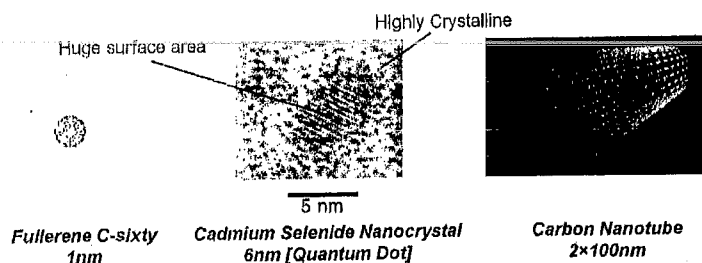
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*The focus of this article is engineered nanoparticles that are intentionally fabricated for their nanoscale properties.*

fabricated for their nanoscale properties. The ASTM Committee on Nanotechnology<sup>1</sup> has defined a nanoparticle as a particle with lengths in two or three dimensions between 1 and 100 nanometers (nm) that may or may not have a size related intensive properties. Nanoparticles can be composed of many different base materials (carbon, silicon, and metals such as gold, cadmium, and selenium, see Figure 1). Nanoparticles also have different shapes: referred to by terms such as nanotubes, nanowires, crystal-line structures such as quantum dots, and fullerenes. Nanoparticles often exhibit very different properties from their respective micron sized bulk materials: greater strength, conductivity, and fluorescence, among other properties. Many more of the atoms in nanoparticles are on the surface, resulting in greater reactivity than bulk materials.

Particles in the nanometer size range do occur both in nature and as an incidental byproduct of existing industrial processes. Nanosized particles are part of the range of atmospheric particles generated by natural events such as volcanic eruptions and forest fires. They also are part of the fumes generated during welding, automobile exhaust, and other industrial combustion processes. One concern about small particles that are less than 10  $\mu\text{m}$  is that they are respirable and reach the alveolar spaces in the lungs. Another concern is that some epidemiological studies suggest that ambient ultrafine particles (<100 nm) may be responsible for adverse respiratory and cardiovascular effects observed during air pollution events, though not all studies show an association (see Oberdorster et al. for a review).<sup>2</sup>

The current nanotechnology revolution differs from past industrial processes because nanomaterials are being created and fabricated from the "bottom up", rather than occurring as a byproduct of other activities. The particles being engineered have different and unexpected properties compared to those of the parent compounds. Since their properties are different when they are small, it is expected that they will have different effects on the



**Figure 1. Types of engineered nanoparticles.** Source: Fullerenes and CNTs - Mstroek on en.wikipedia under GNU Free Documentation license; Quantum Dots - Anthony-Garratt Reed, Peter Allen, and Mounji Bawendi, MIT.

*Any toxic effects of nanoparticles will be very specific to the type of base material, size, substituents, and coatings.*

body and will need to be evaluated separately from the parent bulk compounds for toxicity.

Currently engineered nanoparticles have a limited commercial market though the market is expected to expand rapidly. A database of products currently on the market and said to contain nanomaterial is being maintained by the Woodrow Wilson Institute (see listing of web sites at end of article). Some nanomaterials are used as catalyst supports in catalytic converters; nanosized titanium dioxide particles are used as a component of sunscreens; carbon nanotubes have been used to strengthen tennis rackets; components in silicon chips are reaching the 45–65 nm range. Research and industrial labs are working at the intersection of engineering and biology to extend uses to medicine as well as all areas of engineering. The impact is expected to revolutionize these areas. Government agencies in

the US and Europe are beginning to fund toxicology research to understand the hazards of these materials before they become even more widely available.

#### WHAT ARE THE TOXIC EFFECTS OF NANOMATERIALS TESTED TO DATE?

This article presents an overview of the some of the major areas of testing done to date (see Table 1). A list of web sites and research citations is given at the end of the article for more information.

#### Nanoparticles may be More Toxic than Micron Sized Particles of the Same Material

Any toxic effects of nanoparticles will be very specific to the type of base material, size, substituents, and coatings. One of the earliest observations was that nanoparticles, also called ultrafine particles (<100 nm), showed

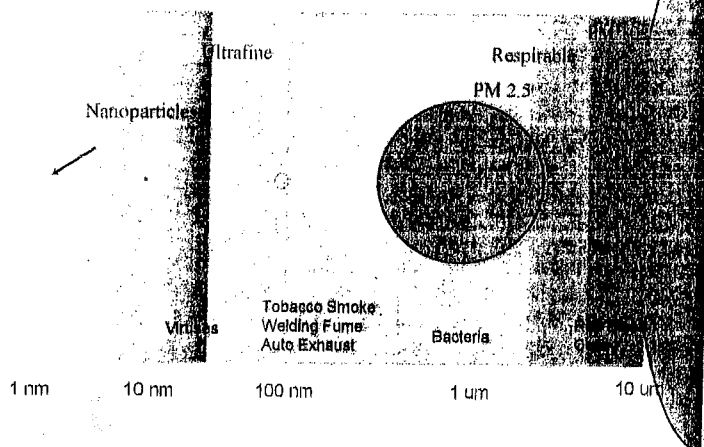
greater toxicity than fine particulates (<2.5  $\mu\text{m}$ ) of the same material on a mass basis. This has been observed with different types of nanoparticles, including titanium dioxide, aluminum trioxide, carbon black, cobalt, and nickel. For example, Oberdorster et al.<sup>3</sup> found that 21 nm titanium dioxide particles produced 43 fold more inflammation (as measured by the influx of polymorphonuclear leucocytes, a type of white blood cell, into the lung) than 250 nm particles based on the same mass instilled into animal lungs. The increase in inflammation is believed to due to the much greater surface area of the small particles for the same mass of material.

Though multiple studies have shown that nanosized particles may be more toxic than micron sized particles, this is not always the case. Intrinsic surface reactivity may also be as important as surface area. Warheit et al.<sup>4</sup> found that the toxicity for cytotoxic crystalline quartz did not relate to particle size, but did relate to surface reactivity as

**Table 1. Toxicological effects of nanoparticles**

Toxicological Effect	Example of Study
Nanoparticles may be toxic to cells in vitro	Cadmium-selenium quantum dots toxic to monkey and human cell lines (cell death)
Cytotoxicity may be modified or reduced by coatings or substituent groups	Cd-Se quantum dots coated with ZnS or polyethylene glycol do not cause cell death during two-week incubation in liver hepatocytes
Nanoparticles may be more toxic than micron sized particles in short-term animal tests	Nanosized titanium dioxide (20 nm) produced 43 fold more inflammation than 250 nm size particles in short-term tests of pulmonary toxicity in rats
Nanoparticles may translocate to other organs in body	Radioactive carbon particles found in liver after six-hour inhalation exposure in rats
Nanoparticles may enter brain through nasal epithelium olfactory neurons	Radioactive carbon reached olfactory bulb, cerebellum, and cerebrum via olfactory neurons in rats
Nanoparticles may cause pulmonary inflammation, granulomas, and fibrosis in short-term animal tests	CNTs cause inflammation, granulomas, and fibrosis after single dose instillation in mice. Also decreased breathing rate and bacterial clearance
Nanoparticle may penetrate skin in isolated skin assays	Quantum dots penetrate to living dermis in isolated pig skin bioassay

## Nanoparticles are smaller than cells



**Figure 2. Size relationship of nanoparticles to human cells. Source: Andrew Maynard, Woodrow Wilson Institute.**

measured by hemoglobin release from cells *in vitro*.

### Nanoparticle Size in Relation to Human Cells

Nanoparticles (<0.1  $\mu\text{m}$ ) are generally similar in size to proteins in the body (see Figure 2). They are considerably smaller than many cells in the body. Human alveolar macrophages are 24  $\mu\text{m}$  in diameter and red blood cells are 7–8  $\mu\text{m}$  in diameter.

### Effect of Substituent Groups on Nanoparticle Toxicity

The ability to be taken up by cells is being used to develop nanosized drug delivery systems and does not inherently indicate toxicity. One study by Goodman et al.<sup>5</sup> found that cellular toxicity depended upon the charge of side chains substituted onto 2 nm gold nanoparticles using tests of cytotoxicity in mammalian and bacterial cells. This research group is currently designing nanoparticles with substituent groups that minimize toxicity.

### Nanoparticles may Translocate Throughout the Body

Once in the body, some types of nanoparticles may have the ability to translocate and be distributed to other organs, including the central nervous system. Silver and carbon nanoparticles all showed systemic availability

after inhalation exposure. Significant amounts of  $^{13}\text{C}$  labeled carbon particles (22–30 nm in diameter) were found in the livers of rats after 6 h of inhalation exposure to 80 or 180  $\mu\text{g}/\text{m}^3$  (Oberdorster et al.<sup>6</sup>). In contrast, only very small amounts of  $^{192}\text{Ir}$  particles (15 nm) were found systemically. Oberdorster et al.<sup>7</sup> also found that inhaled  $^{13}\text{C}$  labeled carbon particles reached the olfactory bulb and also the cerebrum and cerebellum, suggesting that translocation to the brain occurred through the nasal mucosa along the olfactory nerve to the brain. The ability of nanoparticles to move about the body may depend on their chemical reactivity, surface characteristics, and ability to bind to body proteins.

### Skin penetration of nanoparticles

There is currently no consensus about the ability of nanoparticles to penetrate through the skin. Particles in the micrometer range are generally thought to be unable to penetrate through the skin. The outer skin consists of a 10  $\mu\text{m}$  thick, tough layer of dead keratinized cells (stratum corneum) that is difficult to pass for particles, ionic compounds, and water soluble compounds. Tinkle et al.<sup>8</sup> found that 0.5 and 1  $\mu\text{m}$  dextran spheres penetrated “flexed” human skin in an *in vitro* experiment. Particles

penetrated into the epidermis and a few entered the dermis only during flexing of the skin. Particles 2 and 4  $\mu\text{m}$  in diameter did not penetrate. Rymen-Rasmussen et al.<sup>9</sup> also found that nanometer size quantum dots penetrated through pig skin and into living dermis using an *in vitro* pig skin bioassay which is considered a good model for human skin.

Micron sized titanium dioxide (40 nm) is currently being used in sunscreens and cosmetics as sun protection. The nm particles are transparent and do not give the cosmetics the white, chalky appearance that coarser preparations did. The nm particles have been found to penetrate into the stratum corneum and more deeply into hair follicles, and sweat glands than  $\mu\text{m}$  particles though they did not reach the epidermis layer and dermis layers (Laddeman et al.<sup>10</sup>). There is also a concern that nm titanium dioxide particles have higher photo-reactivity than coarser particles and may generate free radicals that can cause cell damage. Some manufacturers have addressed this issue by coating the particles to prevent free radical formation. The FDA initially reviewed available information and determined that nm titanium dioxide particles are not a new ingredient but a specific grade of the original product but has decided to re-evaluate this question.

*Quantum dots (QD)* are nanocrystals containing 1000–100,000 atoms and exhibiting unusual “quantum effects” such as prolonged fluorescence (Figure 1). They are being investigated for use in immunostaining as alternatives to fluorescent dyes. The most commonly used material for the core crystal is cadmium-selenium, which exhibits bright fluorescence and high photostability. Both bulk cadmium and selenium are toxic to cells. One of the primary sites of cadmium toxicity *in vivo* is the liver.

Early studies found that Cd-Se quantum dots were not toxic to immortalized cell lines used for these studies. Recently Shiohara et al.<sup>11</sup> found that three types mercapto-undecanoic acid (MUA) substituted Cd-Se quantum dots decrease viability in three types of cells *in vitro* (monkey kidney, HeLa cells, and human hepatocytes) and

caused cell death after 4–6 h of incubation. One type of MUA-QD was less toxic than the other two. Derfus et al.<sup>12</sup> also found that Cd–Se QDs were toxic to liver hepatocytes if exposed to air or UV light, as a result of oxygen combining with Se and releasing free Cd<sup>2+</sup> from the crystal lattice. They found that coating the Cd–Se QDs with ZnS, polyethylene glycol, or other coatings prevented toxicity during a two-week incubation with hepatocytes. They concluded that Cd–Se QDs can be made nontoxic with appropriate surface coatings but future use *in vivo* must be carefully evaluated to rule out release of Cd<sup>2+</sup> over time.

**Carbon nanotubes (CNT)** can have either single or multiple layers of carbon atoms arranged in a cylinder (Figure 1). Typical dimensions of single wall carbon nanotubes (SWCNT) are about 1–2 nm in diameter and several microns in length. Multi-walled carbon nanotubes (MWCNT) have several concentric layers. CNTs may behave like fibers in the lung. They have properties very different from bulk carbon or graphite. They have great tensile strength and are potentially the strongest, smallest fibers known. CNTs have been tested in short-term animal tests of pulmonary toxicity and the results suggest the potential for lung toxicity though there are questions about the nature of the toxicity observed and the doses used. Lam et al.<sup>13</sup> instilled three types of SWCNTs into rat lungs and found granulomas, a type of cellular accumulation in the lung in which clumps of fibers were surrounded by mononuclear macrophages. In this bioassay, quartz, a dust known to be very toxic to human lungs, also produced lung damage but carbon black did not.

Warheit et al.,<sup>14</sup> using a different type of SWCNT, also found granulomas but did not see increases in other markers of pulmonary inflammation. Quartz produced macrophage accumulation and increased pulmonary inflammation. Warheit et al. interpreted their SWCNT results as possibly of limited physiological relevance but requiring further inhalation studies. Shvedova et al.<sup>15</sup> using more physiologically relevant doses, found granulomas, fibrosis, and increased markers

of inflammation from SWCNTs. SWCNTs also affected lung function: breathing rate and the ability to clear bacteria were decreased. Mitchell et al.<sup>16</sup> conducted a two-week inhalation study in mice exposed to an aerosolized mixture of MWCNTs and other carbon fibers. They did not observe pulmonary damage and did find systemic immune system suppression as measured by antibody and cellular response in the spleen. More extensive inhalation studies are needed and are currently underway in several research centers.

One mitigating factor regarding lung toxicity is that CNTs have a tendency to clump together to form nanoropes, which are large, non-respirable clumps, and may prevent inhalation exposure in many instances (Maynard et al.<sup>17</sup>). The addition of functional groups such as phenyl-sulfite and phenyl-carboxylic acid onto CNTs can decrease toxicity, as demonstrated using *in vitro* tests by Sayes et al.<sup>18</sup> Other *in vitro* tests have found inhibited cell growth and viability. Good recent reviews of CNT toxicity which cover pulmonary toxicity and also *in vitro* testing and environmental considerations are provided by Donaldson et al.<sup>19</sup> and Helland et al.<sup>20</sup> A recent report by Li et al.<sup>21</sup> found that instillation of CNTs produced cardiovascular effects in transgenic arteriosclerosis prone mice; the mice developed accelerated plaque formation after four doses of CNTs over an 8-week period.

**Fullerenes** are another category of carbon based nanoparticles (Figure 1). The most common type has a molecular structure of C<sub>60</sub> which take the shape of a ball shaped cage of carbon particles arranged in pentagons and hexagons. Fullerenes have many potential medical applications as well as applications in industrial coatings and fuel cells, so a number of preliminary toxicology studies have been done. In cell culture, different types of fullerenes produced cell death at concentrations of 1–15 ppm in different mammalian cells when activated by light (as discussed in Colvin<sup>22</sup>). Sayes et al.<sup>23</sup> found that toxicity could be eliminated when carboxyl groups were substituted on the fullerene surface to increase water solubility. Cell death in this study appeared

to be a function of damage to the cell membranes. In an *in vivo* study, Chen et al.<sup>24</sup> found that water soluble polyalkylsulfonated C<sub>60</sub> produced no deaths in rats when given orally but was moderately toxic when administered intraperitoneally (LD<sub>50</sub> = 600 mg/kg). Doses of 100–600 mg/kg also produced an unusual form of kidney toxicity.

Finally, in the first study investigating aquatic toxicology, Oberdorster<sup>25</sup> found that 48 h of exposure to 0.5 and 1.0 ppm of uncoated pure C<sub>60</sub> produced cell membrane lipid peroxidation in the brains of fish (juvenile large mouth bass). The changes in the brain as a result of the short exposure did not appear to affect the behavior of the fish but were an indication of oxidative stress. An additional concern generated by this study is the effects of release of durable carbon nanomaterials into the environment.

#### HOW TO WORK SAFELY WITH NANOMATERIALS

The preliminary conclusions to be drawn from the toxicology studies to date are that some types of nanomaterials can be toxic, if they are not bound in a substrate and they are available to the body. Multiple government organizations are working to fund and assemble toxicology information on these materials. In the interim, researchers must use procedures developed under their Chemical Hygiene Plan that prevent inhalation and dermal exposures because at this time nanotoxicology information is limited. In promulgating the Laboratory Safety Standard, OSHA recognized that many research materials and newly synthesized chemicals have limited or no toxicity information. Using stringent precaution is therefore warranted for these materials (see Table 2).

Based on particle physics and studies of fine atmospheric pollutants, nanoparticles are in size range that remains suspended for days to weeks if released into air. Nanoparticles can be inhaled and will be collected in all regions of the respiratory tract; about 35% will deposit in the deep alveolar region of the lungs (Maynard and Kuempfel<sup>26</sup>). Based on existing data for nanometer

**Table 2. Summary of university best practices**

Prevent inhalation exposure	Use in fume hood, biosafety cabinet, or other exhausted enclosure Synthesis in furnace or reactor: exhaust reactor gasses, purge before opening, provide local exhaust ventilation for emission points, perform part maintenance in fume hood Eliminate use on open lab bench Transport within lab in sealed containers
Prevent dermal exposure	Use sturdy gloves for dry particulate Use gloves resistant to solvent if nanoparticles are in suspension If skin contamination likely, use double gloves or gloves with gauntlets or extended sleeves Use lab coats, preferably disposable Use appropriate eye protection
Prevent laboratory contamination	Wet wipe hood and other lab surfaces after use or at end of day; never sweep or use compressed air for cleaning Use bench liners or HEPA vacuum cleaners as alternatives
Prevent exposure during spills	Have spill kit on hand: wet wipe for dry spills, use appropriate absorbent for spills of suspensions Use HEPA vacuum cleaner for larger spills Use respirator (disposable P100 or elastomeric half-mask with P100 cartridges) if inhalation exposure possible
Nanomaterial waste	Dispose of nanomaterials and nanomaterial-contaminated lab materials as hazardous waste until specific regulations are developed Label waste as nanoscale
Obtain current toxicity information on nanomaterials in use	MSDSs are inaccurate and often report health effects of micron sized materials. Keep current on toxicity of nanomaterials in use in the lab by web searches (ICON, Pub Med, NIOSH)

sized particles and collection efficiency curves, NIOSH has stated that HEPA filters are expected to capture nanoparticles. Moyer<sup>27</sup> tested HEPA respirator cartridges and found acceptable respirator collection efficiency. Kim et al.<sup>28</sup> tested commercial filter media and found acceptable collection efficiency and no detectable particle thermal rebound down to 3 nm using silver nanoparticles.

In the last several years, a number of universities and research laboratories have posted specialized guides for working with nanomaterials on their web sites (see section at end of paper for university best practice web sites). There is a convergence of ideas in these documents regarding interim best practices until more is known about the toxicity of these materials. Working safely with nanomaterials involves following standard procedures that would be followed for any particulate material with known or uncertain toxicity: preventing inhalation, dermal, and ingestion exposure.

Many nanoparticles are synthesized in enclosed reactors or glove boxes.

The enclosures are under vacuum or exhaust ventilation, which prevent exposure during the actual synthesis. Inhalation exposure can occur during additional processing of materials removed from reactors, and this processing should be done in fume hoods, glove boxes, or biosafety cabinets. Manipulation of nanomaterials as free particles or on the lab bench should be avoided. For equipment or processes too large to be enclosed in a fume hood, specialized local exhaust ventilation can be used to capture particles at potential emission points. Material removed from reactor should be in sealed container for transport. In addition, maintenance on reactor parts that may release residual particles in the air should be done in fume hoods or other exhausted enclosures. The synthesis of particles such as quantum dots using sol-gel chemistry should be carried out in ventilated fume hoods or glove boxes. A sol-gel process is a wet chemical technique in which chemical solutions react to produce colloidal particles.

Contamination of lab surfaces should be prevented. Fume hood surfaces

should be wet wiped after each use or at the end of the day. Alternatively use of bench liners would also prevent contamination. In case of spills outside enclosures, wet wiping would be acceptable for small spills. Large spills can be cleaned using a vacuum cleaner fitted with a HEPA filter on the exhaust such as the Nilfisk GM80CR. Respirators with HEPA or P100 cartridges should be available if large spills outside enclosures are a possibility.

Since the ability of nanoparticles to penetrate the skin is uncertain at this point, gloves should be worn when handling particulate and solutions containing particles. A glove having good chemical resistance to any solution the particles are suspended in should be used. If working with dry particulate, a sturdy glove with good integrity should be used. Disposable nitrile gloves commonly used in many labs would provide good protection from nanoparticles for most procedures that do not involve extensive skin contact. Two pairs of gloves can be worn if extensive skin contact is anticipated, as well as gloves with gauntlets or extended sleeve nitrile gloves, to

prevent contamination of lab coats or clothing.

One potential safety concern with nanoparticles is fires and explosions if large quantities of dust are generated during reactions or production. This is expected to become more of a concern when reactions are scaled up to pilot plant or production levels. Both carbonaceous and metal dusts can burn and explode if an oxidant such as air and an ignition source are present. Nanodusts can be anticipated to have a greater potential for explosivity than larger particles. Determination of lower flammability limits using standard test bomb protocols is being planned in Europe.

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#### EXPOSURE MONITORING

Based on the unique characteristics of nanoparticles, many believe that mass is not the appropriate measure of exposure. There also exists a background of

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nanoparticles in air, in the range of 3000–10,000 particles per cc, due to man-made emissions from vehicles and combustion sources and also from natural sources. Groups performing monitoring currently use a suite of instruments to measure particle concentration and size distribution and to characterize particle type. Both NIOSH and the DOE Nanoscale Science Researcher Centers (see web sites at end of article) have outlined air sampling approaches using direct reading instrumentation for particle number and active and passive sampling for electron microscopy analysis (particle characterization). If available, a TSI Scanning Mobility Particle Sizer (SMPS) or Fast Mobility Particle Sizer (FMPS) are also very useful for particle size distribution measurements. The cost of these two instruments is in the \$80,000 range (US dollars).

There are several research groups using a battery of instruments to characterize nanomaterial exposures and publications are starting to appear. Maynard et al.<sup>17</sup> looked at the release of CNTs after synthesis during harvest-

ing from reactors. He found almost no release of fibers when carbon nanotubes were removed from a reactor and transferred into a secondary container. The SWCNT clumped together into nanoropes and remained attached to the substrate as it was removed from the reactor. Maynard et al.<sup>17</sup> also found that it took considerable energy to break up the nanoropes and release them into air: the highest settings on a fluidized bed vortex shaker were needed to produce aerosol release. The type of SWCNT investigated in this study was uncoated with about 30% Fe catalyst remaining as part of the nanoropes.

Bello et al.<sup>29</sup> used the FMPS and electron microscopy analysis to characterize the emissions from a chemical vapor deposition furnace used to grow a CNT “forest” on a silicon chip. Iron deposited on the chip in a previous process served as the catalyst. They found no CNT release during the growth cycle and during the opening of the furnace and removal of the chip. These two studies suggest some processes produce a CNT product that is not easily dispersed. However, researchers are attempting to coat CNT and other nanoparticles with materials that make them less sticky and more easily dispersed; if successful, this would make them more easily aerosolized and require additional care when handling. Also, if the catalyst is aerosolized in the furnace during the growth cycle, there may be release when the furnace is opened.

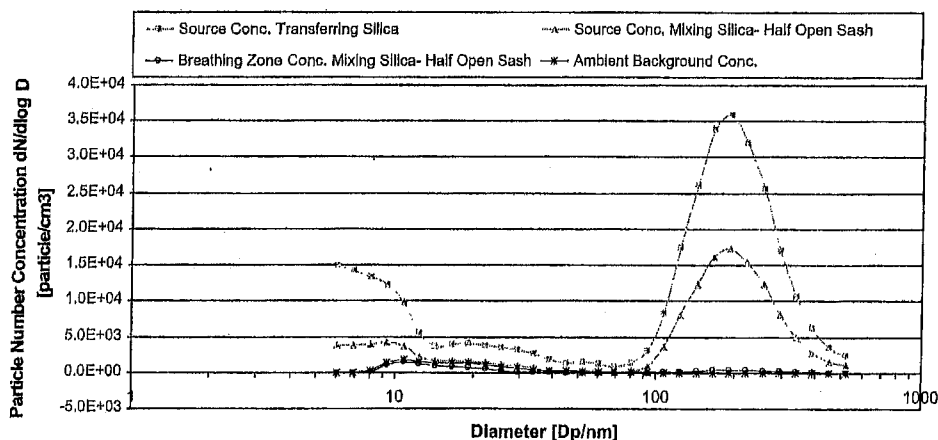


Figure 3. Amorphous silica handling—source concentration inside fume hood vs. breathing zone concentration.

MIT has collaborated with the University of Massachusetts Lowell, Department of Work Environment which has purchased a FMPS as part of a High Rate Nanomanufacturing Project. We used the FMPS to monitor possible emissions from a fume hood during the transfer of gram quantities of amorphous silica (average size 300 nm) in a fume hood operating at 100 fpm. Figure 3 shows that the fume hood contained well: peaks can be seen at the source inside the fume hood but not outside in the breathing zone of the researcher. The U Mass Lowell group (Tsai et al.<sup>30</sup>) has tested other fume hoods and found good containment with hoods operating in the 100 fpm face velocity range and equipped with airfoils and by-passes. However, they observed some release of light density nano alumina during transfer operations at excessively high and low face velocities.

#### GOVERNMENT STANDARDS AND MATERIAL SAFETY DATA SHEETS

There are currently no promulgated government occupational exposure standards for nanomaterials. NIOSH has issued a draft standard for nano and micron sized titanium dioxide, based on animal inhalation studies. They recommend 0.1 mg/m<sup>3</sup> for nano-sized TiO<sub>2</sub> (<100 nm) and 1.5 mg/m<sup>3</sup> for micron sized TiO<sub>2</sub>. The document is currently under revision. The British Standards Institute<sup>31</sup> has recently published benchmark exposure levels for four categories of nanomaterials: fibrous nanomaterials, insoluble nanomaterials, soluble nanomaterials, and nanomaterials for which the bulk material is carcinogenic, mutagenic, asthmagenic, or a reproductive toxin. When occupational health standards are eventually developed, they may take the form of "control bands" for different physical categories of nanomaterials, i.e., different types of exposure controls would be required for different categories. For example, the stringency of controls would be different for the following forms of nanomaterials (from least to most control): solid materials with embedded nanostructures, solid materials with nanostructure bound

to the surface, liquid suspension of nanoparticles, free nanoparticles (dry, dispersible single particles or agglomerates).

One should also be aware that Material Safety Data Sheets (MSDS) may not have accurate information at this point. For example, the MSDSs that accompany some commercially available carbon nanotubes refer to the graphite Permissible Exposure Limit as a relevant exposure standard. Both graphite and carbon nanotubes are composed of carbon arranged in a honeycomb pattern. However, CNTs have very different tensile and conductive properties than graphite. Additionally CNTs are much more toxic in the short-term animal tests that have been performed to date. Consequently, the graphite PEL and toxicity information is not appropriate for MSDSs of CNTs. If not bound in a substrate, CNTs should be treated as potentially toxic fibers and should be handled with appropriate controls as described previously.

#### NANOMATERIAL WASTE MANAGEMENT

As nanotechnology emerges and evolves, potential environmental applications and human health and environmental implications are under consideration by the EPA and local regulators. EPA has a number of different offices coordinating their review of this rapidly evolving technology. The EPA is currently trying a voluntary approach to testing and developing a stewardship program. There are currently no guidelines from the EPA specifically addressing disposal of waste nanomaterials. Some local political subdivisions are considering or have already promulgated local regulations, such as the city of Berkeley.

MIT and other universities are taking a cautious approach to nanowaste management. In order to better understand the characteristics of these waste streams, all waste materials potentially contaminated with nanomaterials are identified and evaluated or collected for special waste disposal. On the label content section the researchers are asked to indicate that it contains nano-

sized particles and indicate base materials and carrier liquids.

The following waste management guidance applies to nanomaterial-bearing waste streams consisting of:

- Pure nanomaterials (e.g., carbon nanotubes)
- Items contaminated with nanomaterials (e.g., wipes/PPE)
- Liquid suspensions containing nanomaterials
- Solid matrixes with nanomaterials that are friable or have a nanostructure loosely attached to the surface such that they can reasonably be expected to break free or leach out when in contact with air or water, or when subjected to reasonably foreseeable mechanical forces.

The guidance does not apply to nanomaterials embedded in a solid matrix that cannot reasonably be expected to break free or leach out when they contact air or water, but would apply to dusts and fines generated when cutting or milling such materials. Researchers are told to never put material from nanomaterial-bearing waste streams into the regular trash or down the drain. If there are any questions, the EHS Office can be called for a waste determination.

Paper, wipes, PPE and other items with loose contamination are collected in a plastic bag or other sealing container stored in the laboratory hood. When the bag is full, close it, it is taken out of the hood, sealed and placed it into a second plastic bag or other sealing container. The outer bag is labeled with the laboratory's proper waste label. The content section of the label must indicate that it contains nanosized particles and specify type.

Currently the disposal requirements for the base materials are considered first when characterizing these materials. If the base material is toxic, such as silver or cadmium, or the carrier is a hazardous waste, such as a flammable solvent or acid, clearly they should carry those identifiers. Many nanoparticles may also be otherwise joined with toxic metals or chemicals. Bulk carbon is considered a flammable solid, so even carbon based nanomaterials should be

collected for determination as hazardous waste characteristics.

#### ADDITIONAL SOURCES OF INFORMATION

Below are additional information sources for nanomaterials. The MIT EHS Office periodically updates the MIT community about significant new studies on important categories of nanomaterials. Many of the articles listed below can be accessed electronically through university libraries if an electronic subscription is available. Web sites are also provided where available.

#### ACKNOWLEDGEMENTS

We would like to acknowledge our collaborators at University of Massachusetts Lowell, Department of Work Environment, Center for High-Rate Nanomanufacturing for bringing the FMPS to MIT, conducting air monitoring in our laboratories, and providing immensely helpful information to our department and our researchers (Dr. Michael Ellenbecker, Dr. Dhimiter Bello, Dr. Kwangseog Ahn, and Dr. Su-Jung (Candace) Tsai).

#### WEB SITES THAT POST CURRENT INFORMATION ABOUT NANOTOXICOLOGY

International Council on Nanotechnology at <http://icon.rice.edu> (accessed 1/28/08).

National Institute for Occupational Safety and Health (NIOSH) Nanotechnology Page at <http://www.cdc.gov/niosh/topics/nanotech/> (accessed 1/28/08).

National Nanotechnology Infrastructure Network (NNIN) at <http://www.nnin.org/> (accessed 1/28/08).

National Center for Biotechnology Information (NCBI) Pub Med at <http://www.ncbi.nlm.gov/entrez> (accessed 1/28/08). [Can search for articles on nanoparticle toxicity.]

Woodrow Wilson Institute. Project on Emerging Nanotechnologies. Con-

sumer Products Inventory. Available at <http://www.nanotechproject.org/inventories/consumer/> (accessed 1/28/08).

#### UNIVERSITY OR RESEARCH LAB WEB SITES WITH GUIDELINES FOR WORKING WITH NANOMATERIALS

DOE Nanoscale Science Researcher Centers. Approach to Nanomaterial ES&H (June 2007). Available at [www.sc.doe.gov/bes/DOE\\_NSRC\\_Approach\\_to\\_Nanomaterial\\_ESH.pdf](http://www.sc.doe.gov/bes/DOE_NSRC_Approach_to_Nanomaterial_ESH.pdf) (accessed 1/28/08).

MIT. Potential Risks of Nanomaterials and How to Safely Handle Materials of Uncertain Toxicity. Available at <http://web.mit.edu/environment/ehs/topic/nanomaterial.html> (accessed 1/28/08).

Texas A&M Engineering. Interim Guideline for Working Safely with Nanotechnology. Available at [http://engineering.tamu.edu/safety/guidelines/Nanotechnology/NANO\\_SafeGuideline.pdf](http://engineering.tamu.edu/safety/guidelines/Nanotechnology/NANO_SafeGuideline.pdf) (accessed 1/28/08).

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