A Guide for the Safe Handling of Engineered and Fabricated Nanomaterials

Wanda L. Greaves-Holmes

Abstract

In the absence of scientific clarity regarding the potential health effects of occupational exposure to nanoparticles, there is a need for guidance in making decisions about hazards, risks, and controls (Schulte & Salmanca-Buentello, 2007). Presently, no guiding principles have been universally accepted for personal protective equipment that is worn to prevent exposure to nanomaterials. The purpose of this article is to survey the literature and determine if research has been completed that validates whether or not occupational exposure to nanomaterials is potentially hazardous to the health of humans.

Introduction

The science of nanotechnology is the manipulation of matter on a near-atomic scale to produce new structures, materials, and devices (NIOSH, 2005b). Nanotechnology and nanosciences are global technologies that can possibly transform the world's economy and its workforce. Work places (such as research laboratories, production or operation facilities) in which nanomaterials are engineered, processed, used, disposed of or recycled are areas of concern, because in these areas workers are initially exposed to nanomaterials.

Every aspect of nanotechnology is catching the attention of governments and business organizations worldwide. The National Science Foundation (NSF, 2007) predicts that nano-related goods and services could be a $1 trillion market in 2015 and will employ 2 million people, 1 million of which will be in the United States (Roco & Bainbridge, 2001). Saniei et al. (2007) believe nanotechnology will be one of the fastest growing industries in history, even larger than the combined telecommunications and information technology industries that started at the beginning of the technology boom in 1998.

Further, the 2008 National Nanotechnology Initiative (NNI) budget request for nanotechnology research and development was over $1.44 billion, an increase of 13 percent from 2007 (The National Science Foundation, 2009b). The growth in NNI investments during the past seven years, along with a total cumulative funding for the NNI since its inception of $8.3 billion, reflects the consistent, strong support of the United States government for nanotechnology (National Science Foundation, 2009c).

Via the universal commercialization of nanosciences, nanotechnology and nanomaterials have dramatically improved the effectiveness of more than 660 existing consumer and industrial products (Woodrow Wilson International Center for Scholars, 2009). Additionally, nanotechnology has substantially affected the growth of new applications, ranging from disease identification and management to remediation of the environment (e.g., superior drug development and expansion, extremely hard nanocoatings, water decontamination, enhanced information and communication technologies, and the production of stronger, lighter materials).

The research for this paper was conducted by summarizing information reported in scholarly, peer-reviewed journals, scientific databases, expert interviews, relevant conferences, and workshops. Other sources of information included national and international governmental and private organizations whose members research environmental health and safety regarding the workplace.

An innovative and relatively new area of research called nanotoxicology, investigates the distinctive biokinetics and toxicological potential of engineered and fabricated nanomaterials. Engineered nanomaterials are generally indentified as ultrafine particulate matter measuring between 1– 100 nm in one dimension. The tendency of these nanoparticles of different shapes (e.g., geodesic spherical domes, crystalline structures, rods, tubes), different chemistries (e.g., carbon, silicon, gold, cadmium (and other metals), possessing different surface characteristics and exhibiting distinctly different properties from their original bulk materials respectively (due to varying mass, charges, solubility, and porosity) to translocate from the location of deposit in the respiratory tract to extra pulmonary organs such as the brain, heart, liver, and bone marrow are being researched, examined, and evaluated using various multidisciplinary approaches. These findings have been anticipated. Numerous epidemiological research studies have documented that acute adverse health effects (e.g., cardiovascular disease) can be related to exposure to ambient airborne particles. Additionally, scientific investigators affirm that ill effects are associated with molecular composition and physical attributes of small particle substances. Case in point: pulmonary exposure to minute quartz particles impairs endothelium and pulmonary muscle and tissues; however, the identical particles slightly coated with clay are less detrimental to the respiratory system. Moreover, the long, thin fibers of asbestos pose a major risk to humans when inhaled. Yet, if these fibers are pulverized into tiny particles with the exact chemical composition, the danger is appreciably reduced. Scientists suggests that synthetic carbon molecules (Carbon 60 molecules also known as buckminsterfullerene, fullerene or buckyballs) have a high potential of being accumulated in animal tissue, but the molecules appear to break down in sunlight, perhaps reducing their possible environmental dangers (Purdue University, 2008).

In the October 2008 issue of ScienceDaily, a featured article highlighted a toxicology study that concluded that some types of nanomaterials (Carbon 60 molecules) can be harmful to animal cells and other living organisms (University of Calgary, 2008). Particle physics scientists and researchers of fine atmospheric pollutants, ultrafine nanoparticulate matter released in to the atmosphere can remain airborne for a significant period of time, be inhaled repeatedly, and then collect in all regions of the respiratory system with over one third of the nanoparticles being deposited in the deepest regions of the lungs. Further, investigators have discovered evidence that indicates nanoparticles can dissolve in the cell membranes, pass into cells, thereby crossing the blood–brain barrier, reform as particles, and alter the cell functions (University of Calgary, 2008).

A 2006 publication distributed by NIOSH entitled, *Approaches to Safe Nanotechnology: Managing the Health and Safety Concerns Associated with Engineered Nanomaterials,* states that inhalation is the most common route of exposure to airborne particles in the workplace. Inhalation is the process by which nanomaterials and oxygen in the air can be brought into the lungs and into close contact with the blood, which then absorbs it and carries it to all parts of the body. At the same time the blood gives up waste matter (such as carbon dioxide), which is carried out of the lungs when exhaled. Investigators also discovered evidence that indicates nanoparticles can dissolve in the cell membranes and pass into cells, thereby crossing the blood–brain barrier, reform as particles, and alter the cell functions (University of Calgary, 2008).

Humans have several defense methods to eradicate unwanted foreign objects. One process involves chemical decomposition for soluble particles and the other mechanism is physical translocation, (i.e., transporting particles from one place to another, for insoluble or low-solubility particles). Soluble ultrafine dusts will dissolve and will not be discussed here, because its effects are highly variable, depending on the composition of the dust. By translocation, insoluble or low-solubility particles deposited in the pulmonary system are eliminated from the respiratory system by transporting them elsewhere in the body. The mucociliary escalator eliminates the coarsest particles, which normally are deposited in the upper lungs, mainly in the tracheobronchial region. The tracheobronchial mucous membranes are covered with ciliated cells that form an escalator and expel the mucus containing the particles into the digestive system. Normally this is an efficient mechanism that eliminates particles from the respiratory tract in less than 24 hours (Kreyling et al., 2002). In the alveolar region, the macrophages will take up the insoluble particles by phagocytosis, a mechanism whereby the macrophages will surround the particles, digest them if they can, and proceed slowly to the mucociliary escalator to eliminate them. This is a relatively slow process, with a half-life of about 700 days in humans (Oberdorster, Oberdoster, & Oberdoster, 2005). However, the efficiency of phagocytosis is heavily dependent on particle shape and size.

Several studies seem to show that unagglomerated ultrafine particles deposited in the alveolar region are not phagocyted efficiently by the macrophages (particularly particles with a diameter of less than 70 nm). However, the macrophages are very efficient for coarser particles in the one to three micrometer range (Tabata and Ikada, 1988). The often inefficient uptake of ultrafine and nanometric dusts by macrophages can lead to a major accumulation of particles if exposure is continued and to greater interaction of these particles with the alveolar epithelial cells. Studies have shown that some ultrafine particles can pass through the epithelium and reach the interstitial tissues (Ferin, Oberdorster, & Penney, 1992; Kreyling & Scheuch, 2000, Kreyling et al., 2002; Borm, 2002; Borm, Schims, & Albrecht, 2004). This phenomenon seems more prevalent in higher species, such as dogs and monkeys, than it does in rodents (Kreyling & Scheuch, 2000; Nikula, Snipes, Barr, Griffith, Henderson, & Mauderly, 1997).

For the workforce, either insoluble or low-solubility nanoparticles in biological fluid are the greatest cause for concern. Due to their minuscule size, scientist have found that nanoparticles posses unique properties. Certain types of nanoparticles can pass through the body's natural defense systems and be transported through the body in insoluble form. Therefore, random nanoparticulate matter can terminate in the bloodstream after penetrating the respiratory or gastrointestinal membranes. These particles circulate to different organs and then collect at specific sites. Certain particles journey along the olfactory nerves and enter the brain, whereas other types penetrate through cell walls and reach the nucleus of the cell. These unusual characteristics could be beneficial as vectors to transmit medication to specific body systems, including the brain. The aforementioned scenario could be repeated and have a toxic effect on the health of workers not utilizing personal protective equipment (PPE.) Usually, in the field of toxicology, the detrimental effects are normally associated with the amount of the substance to which an organism, an animal, or a human is exposed. The greater the mass absorbed, the greater the effect. When investigators studied the behavior or a nanoparticle, it was evident that the measured effects are not related to the mass of the product, which contradicts the classical interpretation of toxicity measurement. Study results are unambiguous, and demonstrate that at equal mass, nanoparticles are more toxic than products of the same chemical composition but of greater size.

Although several authors found a good correlation between the specific surface and the toxic effects, a consensus seems to be emerging in the scientific community that several factors can contribute to the toxicity of nanoparticles; thus, it is currently impossible, with our limited knowledge, to weigh the significance of each of these factors or predict the precise toxicity of each new product.

According to The Institut de recherché Robert-Sauvé en santé et en sécurité du travail (IRSST, 2008), published studies link the observed effects to different nanoparticle parameters: specific surface, number of particles, size and granulometric distribution, concentration, surface dose, surface coverage, degree of agglomeration of the particles and pulmonary deposition site, the "age" of the particles, surface charge, shape, porosity, crystalline structure, electrostatic attraction potential, particle synthesis method, hydrophilic/hydrophobic character and postsynthesis modifications (grafting of organic radicals or surface coverage to prevent aggregation). The presence of certain contaminants, such as metals, can also favor the formation of free radicals and inflammation, while the chemical composition and delivery of surface components, nanoparticles colloidal and surface properties, compartmentation in the lung passages and biopersistence are other factors that add a dimension of complexity to understanding the health effects of nanoparticles and their toxicity (IRSST, 2008).

The slow dissolution of certain nanoparticles or nanoparticle components in the body can become a major factor in their toxicity. These various factors will influence the functional, toxicological, and environmental impact of nanoparticles. Several effects have already been shown in animals. Among these, toxic effects have been identified in several organs (heart, lungs, kidneys, reproductive system), as well as genotoxicity and cytotoxicity. For example, some particles cause granulomas, fibrosis, and tumoural reactions in the lungs. Thus, titanium dioxide, a substance recognized as having low toxicity, shows high pulmonary toxicity on the nanoscale in some studies and no (or almost no) effects in other studies. In general, the toxicological data specific to nanoparticles remains limited, often rendering quantitative risk assessment difficult due to the small number of studies for most substances, the short exposure periods, the different composition of the nanoparticles tested (diameter, length, and agglomeration), or the often unusual exposure route in the work environment. Additional studies (absorption, biopersistence, carcinogenicity, translocation to other tissues or organs, etc.) are necessary for quantitative assessment of the risk associated with inhalation exposure and percutaneous exposure of workers (Ostiguy, Soucy, Lapointe, Woods, Menard, & Trottier, 2008).

Although major trends could emerge that show that nanomaterials are harmless to humans, this author suggests that precautions should be established. Presently, there are no universally standardized, published guidelines or regulations for the safe handling of engineered nanomaterials. Research is inconclusive as to whether or not engineered nanoparticles may pose risk to human health because of various compositions, sizes, and ability to cross mammal's cell membranes. Engineered nanomaterials may exhibit higher toxicity due to their size compared to larger particles of the same composition. Current information about risks associated with nanoparticle exposure is limited. Until irrefutable evidence is available regarding the risks associated with nanomaterials, voluntary precautions for the workplace are highly recommended.

Risk assessments and control strategies for nanotechnology research will be based on the most current toxicological data, exposure assessments, and exposure control information available from The National Institute for Occupational Safety and Health (NIOSH), Nanosafe of the United States Environmental Protection Agency (EPA), The Institut de recherche Robert-Sauvé en santé et en sécurité du travail (IRSST), and the National Institutes of Health (NIH), which were used to formulate these voluntary guidelines. "Approaches to Safe Nanotechnology: A Informational Exchange" published by NIOSH (2006), Nanosafe's procedures, (2008), and the European Agency for Safety and Health at Work literature (2009), suggest the following workplace practices, which may decrease the risk of human exposure to nanomaterials.

Manufacturing Controls

Strict control of airborne nanoparticles can be accomplished by using conventional capture exhaust ventilation, such as chemical fume hoods. Glove box containment is another effective method. Passing capture exhaust through a HEPA filter will provide protection against release of nanoparticles into the environment. Some actions that would require manufacturing controls include the following:

1. Working with nanomaterial in a liquid media during pouring or agitation, which could release aerosols size nanoparticles.
2. Fabricating nanoparticles.
3. Handling nanomaterials powder.
4. Maintenance or cleaning of equipment used to produce nanomaterials.

Preventing inhalation, skin exposure, and ingestion are paramount if workers are to work safely with nanomaterials. This involves following standard procedures that should be followed for any particulate material with known or uncertain toxicity. Because nanoparticles are so minute, these particles follow airstreams more easily than do larger particles. Control of airborne exposure to nanoparticles can be accomplished mainly by using engineering controls that are similar to those used for general aerosols and vapors. Nanomaterials can be easily collected and retained in standard ventilated enclosures, such as fume hoods. Additionally, nanoparticles are readily collected by HEPA filters. Respirators with HEPA filters are sufficient protection for nanoparticles in case of immense spills. Many nanomaterials are synthesized in enclosed reactors or glove boxes. These enclosures are under vacuum or exhaust ventilation, which prevent exposure during the actual synthesis. Inhalation exposure could occur during additional processing of materials removed from reactors; this processing should be done in fume hoods. In addition, maintenance on reactor parts, which could release residual particles in the air should be done in fume hoods. Another process, the synthesis of particles using sol-gel chemistry, should be carried out in ventilated fume hoods or glove boxes. Good work practices will help minimize exposure to nanomaterials. These work practices are consistent with good laboratory practices in general, for example,

1. Avoiding direct contact with nanomaterials, especially when airborne or in liquid media during a pouring and/or mixing process with a high degree of agitation.
2. Wearing FFP3 type masks or powered respirators incorporating helmets equipped with H14 high efficiency particulate air (HEPA) filters.
3. Installing and using efficient exhaust systems with particle filtration and

ventilation system filters to minimize free-flowing airborne ultrafine particles.

4. Using a sturdy glove with good integrity is imperative when working with dry, ultrafine particulate matter. Using two pairs of disposable nitrile gloves is strongly recommended.

5. Wearing protective eye wear (e.g., safety goggles).

6. Wearing protective clothing and safety shoes.

7. Utilizing ULPA filters (United Lightning Protection Association) to minimize combustion.

8. Prohibiting storage or consumption of food or drink in areas where nanomaterials are handled.

9. Prohibiting application of cosmetics, etc. in areas where nanomaterials are handled.

10. Requiring all employees to wash their hands before leaving the work area and after removing protective gloves.

11. Removing lab coats, which can easily become contaminated, before leaving the lab or workplace.

12. Making sure that workers avoid touching their face or other exposed skin after working with nanomaterials and prior to hand washing.

13. Labeling all containers with nanomaterials consistent with existing laboratory requirements.

14. Cleaning of any areas where nanomaterials could be must be done via wet wiping or HEPA vacuuming. Dry sweeping or using compressed air is prohibited.

15. Disposing of contaminated cleaning materials must comply with hazardous waste disposal policies.

Fire and Explosions

Other potential safety concerns regarding nanoparticles are fires and explosions, which can happen if large quantities of dust are generated during production. This is expected to become more of a concern when reactions are scaled up to pilot plant or production levels. Scientific evidence concludes that carbonaceous and metal dusts can burn and explode if an oxidant such as air and an ignition source are present.

Conclusion

Nanotechnology is a dynamic and rapidly growing field that offers the promise of technologically based innovations that will substantially improve the quality of life for all humans. The preliminary data currently available on some products reveals that engineered nanoparticles must be handled with care and that workers' exposure must be minimized, because effects from such particles are extremely variable from one product to another. Therefore, a comprehensive understanding of the possible drawbacks of nanotechnology is critical to realizing the significant benefits of nanotechnology. The majority of the initial nanomaterials research has focused on the probable hazards and risks of nanotechnology-based manufacturing. Although, toxicological research for nanotechnology is in its formative years, concerns about potential risks to the health and safety of workers will require definitive answers.

Researchers' questions should be focused on manufacturing practices, procedures, and controls for the present and future uses of nanotechnology. Yet another area of interest is the environment. What is the fate of the environment when nanomaterials are disposed? What does "appropriate" disposal mean as it relates to the field of nanotechnology? What is obvious; however, is that the nanotechnology manufacturing industry must identify, develop, and implement an optimum approach for protecting both its employees and the public at large. One promising option indicates that researchers may be able to "engineer out" unacceptable levels of toxicity in nanomaterials. If this undertaking comes to fruition, then the industry will be able to minimize the potentially negative implications to its workers and the environmental impact of nanomaterial-based manufacturing and products.

According to the documents previously reviewed, toxic effects on living organisms as well as the unique physicochemical characteristics of nanomaterials validate the immediate use of personal protective equipment, etc. to limit exposure and protect the health of potentially exposed individuals. The introduction of strict universally standardized guidelines and procedures to prevent any risk of occupational disease in researchers, students, or workers who synthesize, transform, or use nanoparticles should be introduced *immediately*. A scientific approach to the identification, assessment, and mitigation of the risks posed by nanomaterial manufacturing and commercialization will protect the public, the environment, and industry, thereby ensuring that the benefits of nanotechnology are shared by all.

Wanda L. Greaves-Holmes is a doctoral student at the University of Central Florida, Orlando.

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