



Engineered nanoparticles: safer substitutes for toxic materials, or a new hazard?

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ABSTRACT

Nanotechnology has the potential for the development of new materials and processes that can substitute for toxic materials now used in industry. Excitement over this possibility is tempered, however, by the potential adverse environmental health and safety aspects of the new nanomaterials. Although a few examples from the literature are encouraging, *e.g.*, wire and cable insulation, great care must be taken to perform complete alternatives assessment evaluations of any new nanotechnology-enabled product before its adoption.

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1. Introduction

Nanotechnology is a rapidly-growing field that shows great promise in many disciplines, but it is also one that has engendered considerable concern in the field of occupational and environmental health and safety. The intersection between the possible benefits of nanotechnology and its risks was the subject of a recent Special Issue of the Journal (Helland and Kastenholz, 2008). There seems to be a general consensus that the use of engineered nanoparticles (ENPs) is likely to bring great benefit to society. Researchers are pursuing new applications in fields as diverse as medicine, electronics, textiles, energy, and construction; ENPs with a high potential for successful industrial use include carbon-based materials (*e.g.*, carbon nanotubes, fullerenes), nanocomposites, metals and metal oxides, biological nanomaterials, nano glasses and nano ceramics (Bauer et al., 2008).

Three terms frequently are used interchangeably, but have distinct definitions, *i.e.*, *nanotechnology*, *nanomaterial*, and *nanoparticle*. The following are generally accepted consensus definitions of these terms. According to the National Nanotechnology Initiative (NSTC, 2007),

Nanotechnology is the understanding and control of matter at dimensions between approximately 1 and 100 nm, where unique phenomena enable novel applications. Encompassing nanoscale

science, engineering, and technology, nanotechnology involves imaging, measuring, modeling, and manipulating matter at this length scale.

This definition has also been adapted by the International Standards Organization (ISO, 2008).

Based on the above definition, it follows that a nanomaterial is any material consisting of, or containing, structures with at least one dimension between 1 and 100 nm. It also follows that a nanoparticle is an individual particle of matter with at least one dimension in the 1–100 nm size range.

The 100 nm diameter given as the upper limit for a particle to be defined as a nanoparticle should not be taken as a strict cut-off. Since aerosols typically have a log-normal size distribution (Hinds, 1991), an aerosol whose median diameter is smaller than 100 nm may well have a significant number of particles larger than 100 nm. In addition, particles in the nanometer size range have very high mobility due to Brownian motion, and can agglomerate quickly soon after they are generated.

There is general agreement among scientists that particles in the nanometer size range fall into three categories. Naturally-occurring nanoparticles are nanoparticles in the nanometer size range that are found in nature, such as particles released by volcanic eruptions, particles produced by forest fires, salt particles produced by oceanic wave action, etc. Industrial nanoparticles are particles in the nanometer size range produced as *unwanted byproducts* of our modern industrial society. Common examples include welding fume, diesel exhaust, combustion smoke, etc. Finally, engineered

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nanoparticles are particles in the nanometer size range produced specifically for a purpose – *i.e.*, they are *engineered* to be in the nanometer size range. Engineered nanoparticles range from the very simple (*e.g.*, carbon black) to the very sophisticated (*e.g.*, drug delivery nanospheres). They can be spherical (quantum dots), cylindrical (carbon nanotubes), plate-shaped (nanoclay), or irregular (nanoalumina).

2. Benefits and risks associated with engineered nanoparticles

With nanotechnology moving from development to commercialization at a more rapid rate, so too are calls increasing for a more comprehensive understanding of the production costs, environmental and occupational health risks, and broader societal impacts associated with various nanomanufacturing processes. Commercialization of nanotechnology is proceeding quickly, with over 1000 products containing nanoparticles identified in commerce (WWICS, 2009). Global spending in 2006 was cited at more than 12 billion U.S. dollars (Maynard, 2007). However, this enormous investment dwarfs the funding dedicated to the environmental health and safety (EHS) implications of nanotechnology (Maynard *et al.*, 2006). There are indications that a range of engineered nanomaterials, including nanoparticles, agglomerates of nanoparticles, and particles of nanostructured materials, are likely to present potential risks to human health and the environment. Possible negative properties of these materials include their ability to penetrate dermal barriers, cross cell membranes, travel neuronal pathways, breach the gas exchange regions of the lung, travel from the lung throughout the body, and interact at the molecular level (NIOSH, 2007).

Several recent articles have investigated the toxicity of carbon nanotubes (CNTs) (Donaldson *et al.*, 2006; Erdely *et al.*, 2008; Kane and Hurt, 2008; Kisin *et al.*, 2007; Lam *et al.*, 2006, 2004; Li *et al.*, 2007; Miyawaki *et al.*, 2008; Poland *et al.*, 2008; Shvedova *et al.*, 2008a,b,c, 2005; Takagi *et al.*, 2008; Warheit *et al.*, 2004; Ma-Hock *et al.*, 2009). This literature indicates that there may be significant health effects associated with exposure to CNTs, including granulomatous pneumonia, oxidative stress, acute inflammatory/cytokine responses, fibrosis, and decrease in pulmonary function, and cardiac tissue inflammation. Recent studies findings precursors of mesothelioma following the peritoneal instillation of CNTs in mice (Poland *et al.*, 2008; Takagi *et al.*, 2008) are of particular concern, since mesothelioma is fatal cancer known to be caused by exposure to asbestos. CNTs are fibrous particles with morphology similar to asbestos but with diameters two orders smaller than asbestos.

Given such concerns for the potential toxicity of ENPs, attention must be paid to the potential for exposure to these materials. Occupational exposures are possible during the manufacture of the ENP and during its incorporation into a product. Environmental exposures may occur during manufacturing, product use, and when the product is disposed of. There is concern both for inhalation and dermal exposure. Currently, there are no exposure standards specifically aimed at ENPs in either the occupational or the general environment.

Such concerns are leading to more public calls for increased attention to environmental health and safety issues related to this emerging technology (Maynard *et al.*, 2006; Maynard, 2006). In September 2006, the U.S. House Committee on Science expressed its desire for greater federal research on and coordinated action to address the potential EHS risks of nanotechnology (Committee on Science, 2006). The U.S. Environmental Protection Agency has announced its intent to develop a roadmap for EHS research needs (EPA, 2007). The National Institute for Occupational Safety and Health (NIOSH) has provided an overview of the research undertaken at that

agency, along with summaries of accomplishments and suggestions for additional research needs (NIOSH, 2007). Although NIOSH has suggested preliminary guidelines for working safely with nanomaterials (NIOSH, 2008), research clearly is needed to define risks and provide guidance for safe handling of nanomaterials and to minimize workplace exposure. Various other U.S. government agencies are involved in contributions to the EHS research effort, and an overview of the primary EHS research and information needs recently was developed by the National Science and Technology Council (NSTC) of the U.S. National Nanotechnology Initiative to guide the vast effort deemed necessary to ensure responsible development of nanotechnology (NSTC, 2006).

3. Can engineered nanoparticles substitute for toxic chemicals?

As discussed above, ENPs are being developed for many industrial applications. Given the evidence for toxicity of at least some ENPs and the potential for occupational and environmental exposures, the question arises as to whether it is possible to substitute such particles for other, more toxic chemicals currently in use in various applications, or whether the use of ENPs or, more broadly, nanotechnology (NT) will likely increase the risk associated with these products.

In an attempt to address this important question, this Section will first review some basic concepts underlying substitution, then look at a few examples of substitutions involving ENPs as documented in the literature, and finally explore in some detail a current ENP substitution research project involving the use of nanoclays.

3.1. Substitution as applied to nanomaterials

Fiedeler and his colleagues at the European Technology Assessment Group (ETAG) make the important point that ENPs and NT must be looked at differently from simple chemical substitution (Fiedeler, 2007):

The original meaning of chemical substitution is quite clear and narrow: one chemical substance is replaced by another, for whatever reason (availability, costs, requirements).

Due to the fact that NT is neither a group of substances nor a group of products but an enabling technology the way NT can provide solutions is more fundamental than just replacing the function of the substitute. It is assumed that NT provides new effects which are not based on chemical properties of the related material but on the physical properties caused by its size and shape. It can be used to develop completely different processes or different products which serve the same purpose but in a completely different way.

Given this necessarily broader definition of substitution as it relates to NT and ENPs, it is likely that any practical use of ENPs as a replacement for a more hazardous material will encompass aspects of both *material substitution* and *process change*. In other words, the successful use of ENPs as safer substitutes likely will entail substantial changes in the overall production process and final product, as opposed to a similar “drop-in” material substitution. Such large fundamental changes in production processes will make the process of evaluating the relative health and safety impact of the current process and the proposed change much more difficult than is the case when a simple chemical substitution is contemplated. The alternatives assessment process will likely have to assess the known adverse impacts of the current process against what might be very limited data for the NT-enabled alternative.

It is thus important to use a comprehensive alternatives assessment strategy when evaluating NT-enabled alternatives. The

Lowell Center for Sustainable Production (LCSP) has devoted much attention to this topic in recent years, and has published an Alternative Assessment Framework that outlines the essential elements of a comprehensive assessment approach (Rossi et al., 2006):

At the base of the Framework is the **Foundation**, where values are made explicit by clearly articulating the Principles, Goals, and Rules that guide decisions made during the assessment of alternatives. At the center of the Framework is the **Assessment Processes**—the methods, tools, and criteria used to evaluate which chemicals, materials, or products are safer and socially preferable. The Comparative Assessment Process and the Design Assessment Process are two separate yet overlapping tracks, depending on whether the subject of evaluation is an existing product or a product under development. Necessary to the Assessment Process are the **Evaluation Modules**, which evaluate the economic feasibility, technical performance, human health and environment impacts, and social justice impacts of alternatives.

Beyond alternatives assessment, it will also be important to subject ENP substitution to a full life cycle assessment (LCA). Bauer et al. outline the required elements in the application of LCA to ENPs, and give examples of how it might be used (Bauer et al., 2008); von Gleich et al. suggest a three-tiered assessment approach that incorporates elements of alternatives and life cycle assessment (von Gleich et al., 2008).

3.2. Examples from the literature

A review of the literature reveals very few examples where ENP substitution has made its way into commerce, with the notable exception of medical applications. Nanoparticles are rapidly being developed for many medical applications (Salata, 2004). Some of these new applications are meant to replace others that require the use of hazardous chemicals. The development of nanoparticle-based drug delivery systems for cancer therapy is receiving much attention, because of the widespread, highly-debilitating side effects of drugs now used for cancer treatment. One recent example is research conducted at Washington University into the use of gold nanocages (Skrabalak et al., 2008) for cancer treatment (Chen et al., 2010). The nanocages are first coated with polyethylene glycol (PEG) for biocompatibility and, when injected into the bloodstream, collect preferentially in tumors. They are then irradiated with a laser beam, tuned to a frequency that penetrates body tissues but is absorbed by the nanocages. The absorbed light heats the nanocages, which kills the surrounding tumor cells. This example illustrates the type of advantages the use of ENPs might bring to medicine. There is little in the literature, however, that discusses any potential adverse side effects that might be caused by the ENP due specifically to its small size.

There are limited examples in the published literature of ENPs being successfully used as substitutes for toxic chemicals in industrial applications, and none of the available examples have been subjected to the comprehensive alternatives and life cycle assessments described in Section 3.1. One area that holds some promise is the development of substitutes for solvents. While it is probably not possible to directly substitute an ENP for a solvent, ENPs may be a *component* of a water-based system that substitutes for a solvent-based one. For example, some paint manufacturers claim that nanoparticles are a component of a water-based paint system that can offer similar characteristics to their solvent-based paint products. Incorporation of zinc oxide or titanium dioxide nanoparticles into the formulation may make the paint surface more durable, allowing for thinner paint coatings and an overall reduction in chemical use (Fiedeler, 2007).

To reduce biofouling in such applications as ship hulls typically requires the use of paints incorporating toxic agents such as tributyl tin. If the surface adhesion properties could be changed, the fouling agents may be kept from ever reaching the surface and obviate the need to kill them. The incorporation of nanoparticles into the paint may reduce adhesion through what is commonly called the lotus effect, since lotus leaves are known to readily shed water droplets. Cheng has shown that the presence of nanometer-scale hairlike structures on the lotus leaf surface are responsible for the very high contact angle that leads to water shedding (Cheng et al., 2006). If a marine paint could be developed that incorporated similar structures, the use of tributyl tin could be eliminated.

Another example is the use of nano-emulsions of chemicals in water as a cleaning agent and as a substitute for perchloroethylene used in dry cleaning. For example, EPA recently funded an SBIR project to "...develop a non-toxic nanoemulsion for decontamination of facilities and equipment contaminated with anthrax. The nanoemulsion is an oil-in-water emulsion with broad-spectrum antimicrobial activity optimized for decontamination of *Bacillus anthracis*" (Hamouda, 2006).

One area that is the subject of recent research is the use of nanoclays as part of a package designed to substitute for several hazardous chemicals used in wire and cable insulation. Since this work was performed in our laboratories with partial funding from the Toxics Use Reduction Institute, it will be described in more detail in order to shed some light on the process needed to develop an ENP substitute.

3.2.1. Introduction and background

Wire and cable jackets typically are made of polyvinyl chloride (PVC) and include a plasticizer for flexibility and lead compounds for heat stabilization. Lead-based heat stabilizers are commonly used in the United States because they are inexpensive and very effective at stabilizing PVC, especially when the wire and cable insulation is wet. Although alternative lead-free formulations are now commercially-available, they are more expensive than the lead-based products and may not offer the levels of stabilization required for safe use in highly demanding applications. Some contain other toxic heavy metals (barium or cadmium), some contain organotin (high performance but potentially toxic due to impurities and definitely more expensive than lead), and some contain relatively benign materials but have relatively poor heat-stabilizing properties (calcium, magnesium and zinc-based stabilizers). To summarize what is now available, it would appear that commercially-based lead-free alternatives do not yet equal the performance and cost of lead-based systems.

Analysis of the data collected in Massachusetts under the Toxics Use Reduction Act (TURA) indicates that Massachusetts firms used almost 3.5 million pounds of lead compounds in 1999 in wire and cable insulation. Due likely to reduced wire and cable production in the Commonwealth, this number dropped to 300,000 pounds in 2007.¹

In addition to lead, PVC wire and cable insulation commonly contains phthalates; plasticizers provide flexibility to PVC, and phthalates are used because they are relatively inexpensive and effective. A typical wire and cable insulation can contain up to 30% phthalates by weight. Unfortunately, the weight of evidence strongly suggests that phthalates are endocrine disruptors (see for example (Hiroshawa et al., 2006)), and their use is now restricted or banned in many jurisdictions and applications.

¹ Massachusetts Toxics Use Reduction data available at <http://turadata.turi.org/>.

3.2.2. Work in progress

Research by Schmidt studied whether a more environmentally-acceptable alternative could be developed to replace both the lead and the phthalates in wire and cable insulation. Schmidt investigated the use of a combination of alkylammonium-modified clay and an epoxidized linseed oil (ELO) plasticizer with various heavy metal free heat stabilizers could substitute for lead and phthalates (Dorairaju et al., 2008). In processing, the clay disperses throughout the polymer in the form of nanometer-sized sheets. The research tested whether the nanoclay, when combined with ELO and non-lead heat stabilizers, would be able to offer the needed combination of heat and process stability, coupled with appropriate mechanical and fire properties. The theory was based on the following factors:

- Alkylammonium-modified nanoclays, when used in PVC, reduce its process and heat stability but enhance its mechanical, barrier and fire properties;
- ELO is known to increase PVC heat stability and to interact favorably with the nanoclay;
- Epoxy plasticizers such as ELO are subjected to hydrolysis, which may cause them to become incompatible with PVC over time; however, favorable interactions with the nanoclay coupled with nanoclay-enhanced barrier properties that reduce moisture ingress may enhance the long-term stability of the ELO; and
- Although PVC is inherently a poor fuel, the presence of well-dispersed nanoclay may enhance the flame retardance of the new formulation.

Nanoclay, or montmorillonite, is a naturally-occurring material (de Paiva et al., 2008; Hofmann, 1968; Uddin, 2008). While nanoclay is a non-renewable resource, it is widely abundant in surface deposits and thus can be utilized with relatively minor environmental impact, especially when compared to the processing required to produce lead salts. One important property of nanoclays produced commercially for nanocomposite formation is that, in the bulk dry powder form, individual particles are in the micrometer size range; it is only when the powder is processed with a polymer that each micrometer-sized particle disperses into nanometer-sized particles. Nanoclay is a type of nanomaterial which is difficult to be dispersed to individual airborne clay nanosheets during processing. Thus, the related occupational exposures and environmental releases during processing nanoclay will primarily involve the larger particles, not those in the nanometer size range. However, some other nanomaterials with easy dispersion properties can cause more serious occupational exposure and environmental release than the same material in the micrometer size range, so each scenario must be individually evaluated. Nanoclay is inexpensive (~\$3/lb); the toxicity of nanoclay has not been studied widely, but the information available indicates that it is relatively benign (IPCS, 2005); after a thorough review, the Cosmetic Ingredient Review Expert Panel approved montmorillonite for use as an ingredient in cosmetics (Elmore, 2003). ELO is a bio-based product which is biodegradable and FDA approved for food packaging (FDA, 2010). These factors all lead to the suggestion that nanocomposite formation in the presence of a properly chosen additive package may allow for the replacement of lead in wire and cable insulation, provided, of course, that the required mechanical and chemical properties are present.

Schmidt first investigated the use of nanoclay as a means of enhancing the properties of lead-free, phthalate-plasticized medical grade PVC. Test results found that a nanocomposite of PVC and 2% nanoclay by weight provided "...inherent flame retardance, due to formation of silicate char once burning begins at an exposed surface," and that the desirable mechanical properties

were retained so long as the clay content was kept low (Francis and Schmidt, 2006).

Schmidt then found that a combination of nanoclay, non-lead heat stabilizer (Ca, Mg, and/or Zn based), and ELO were able to provide heat stability, fire protection and flexibility in a single lead- and phthalate-free additive package. This leads to the hope that a commercial product containing an appropriate combination of nanoclay, a relatively non-toxic metal salt, and ELO has the potential to replace lead and phthalates in wire and cable insulation.

3.2.3. Summary

Since this approach is still in the research phase, it is not possible at this time to perform complete alternatives or life cycle assessment. It seems certain that the substitution of nanoclay and ELO for lead and phthalates in wire and cable insulation will result in a less hazardous product, although questions of economic and technical feasibility remain not fully answered. Nonetheless, this is an excellent example of the potential for the environmentally-advantageous use of a nanomaterial.

4. Conclusions

Although there are few examples of ENPs now being used as substitutes for more hazardous chemicals in industrial settings, that situation is likely to change rapidly. The very large current investment in ENP research and development holds the promise for many more such possible substitutions reaching the commercial stage in the near future.

The possible use of ENPs as substitutes for toxic materials in manufacturing holds great promise, but also many risks. For every possible application, alternatives assessment tools, such as the LCSP Alternative Assessment Framework, must be used to carefully analyze the risks and benefits. In the near future for most cases, such assessments will be made more difficult because the risks of the current process will be well-known but the risks associated with the ENP will not have been fully studied. In addition, effective measures for the control of exposure to nanomaterials are under development, as well as the end of life treatment for nanotechnology-enabled products. Such developments will help to overcome the challenges currently experienced when considering the use of nanomaterials and since well-controlled nanomaterials can successfully substitute for the current use of some toxic materials even with unanswered questions as to their toxicity. However, it is recommended at the present that a precautionary approach be taken, and that such substitutions be made only in cases where the ENP clearly represents an improvement over the current materials being used, and where nanoparticle releases to the environment can be controlled.

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