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Short report

The 5 principles of "Design for Safer Nanotechnology"

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ABSTRACT

Nanoparticles have been incorporated in hundreds of different types of products, and the novel properties of nanomaterials offer great promise to provide new technological breakthroughs. However, nanotechnology is an emerging technology which has potential health and safety risks throughout its product life cycle. The health risk of a nanoparticle is a function of both its hazard to human health and its exposure potential. It is prudent for companies to try to mitigate the potential risks of nanoparticles during the design stage rather than downstream during manufacturing or customer use. The intent of this paper is to propose five design principles for product designers to use during the design stage for products that contain nanoparticles. By using these design principles, the health risk of the nanoparticle may be mitigated by potentially lowering the hazard and/or the exposure potential of the nanoparticle. These proposed design principles are largely untested and are offered as an initial framework that will require more testing, validation, and refinement.

1. Introduction

Nanotechnology involves the manipulation of matter on a near atomic scale to produce new structures, devices, and materials. Nanoparticles are particles that have at least one dimension in the range of 1–100 nm. For reference, the diameter of the human hair is approximately 80,000 nm. At the nanoscale, fundamental mechanical, electrical, optical, and other properties can significantly differ from their bulk material counterparts.

The novel properties of nanomaterials offer great promise to provide new technological breakthroughs. Nanotechnology has been explored for creating lighter and stronger materials, for cleaning contaminated groundwater, for replacing toxic chemicals in various applications, for enhancing solar cell efficiency, and for targeted cancer treatment. Nanotechnology is already used in hundreds of products across various industries such as electronics, healthcare, chemicals, cosmetics, materials, and energy. In 2007, there were $147 billion worth of nano-enabled products produced, and this figure is estimated to increase to $3.1 trillion in 2015 [1]. If a product designer has not yet encountered nanoparticles in their products, then there is a high probability that he/she will in the very near future.

However, there have been numerous studies that have raised concerns regarding the health hazards of certain nanoparticles, such as carbon nanotubes [2] and quantum dots [3]. The health risk of a nanoparticle is a function of both its hazard to human health and its exposure potential. The hazard or toxicity of a nanoparticle is the ability for the substance to cause injury, illness, or death to humans. The hazard of a substance is assessed by understanding the relationship between the dose of the substance and the human acute and chronic responses to the substance. The exposure potential of a nanoparticle is a function of its bioavailability to humans through inhalation, ingestion, and dermal pathways as well as its ability to accumulate, persist, and translocate within the environment and the human body. Products that contain hazardous nanoparticles may create potential health and safety risks throughout the product life cycle, including stages such as material processing, transportation, manufacture, use, and disposal of products containing nanoparticles.

For example, carbon nanotubes can be used as an intercalation medium to increase the electrical storage capacity of lithium ion secondary batteries. Exposure to carbon nanotubes can occur during the synthesis and recovery phase of the carbon nanotube production process. During the battery production process, there is potential for carbon nanotube emission until the battery cells are sealed. Carbon nanotube release during product use is unlikely; however it is possible in the case of faulty operation by the user or from irregular recharge attempts. Finally, there is potential carbon nanotube exposure at product end-of-life during either recycling or disposal activities. Recycling processes break down the structure in which the carbon nanotubes are fixed within a battery. These processes generate dust, and carbon nanotubes could be dispersed in air [4].

Since nanotechnology is an emerging technology, many companies are now just beginning to develop production processes

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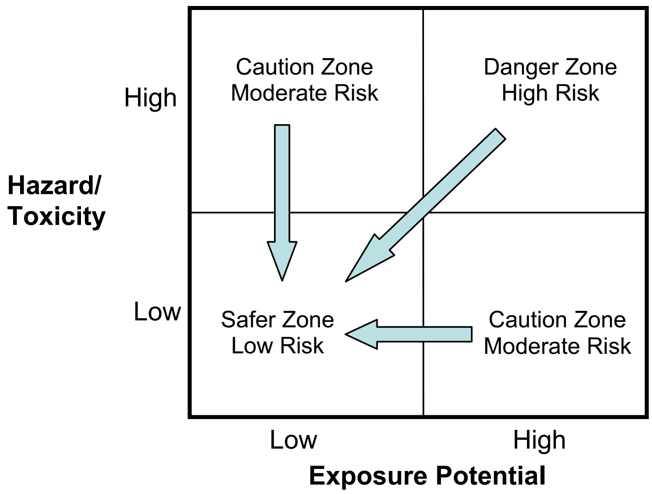

Fig. 1. Nanotechnology risk mitigation matrix.

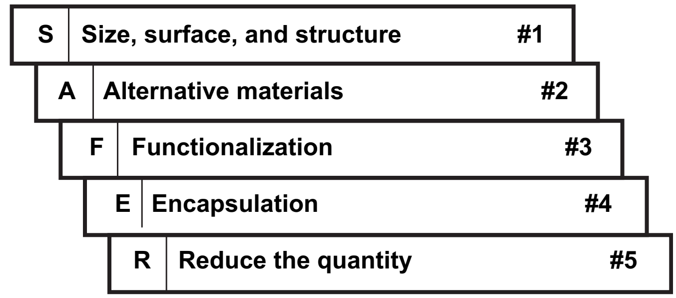

Fig. 2. The five principles of safer nanotechnology.

for incorporating nanoparticles into products. A window of opportunity now exists to reduce or eliminate risks out of these new nanotechnology products and processes. With the focus on risk mitigation, the industry can put this emerging technology onto a path of sustainability [5]. The scientific community faces many challenges to help support the nanotechnology industry to minimize risks and maximize benefits. These challenges include developing robust systems for predicting and evaluating the health and environmental impact of nanoparticles over their entire life cycle [6].

2. Methodology

There are two approaches to achieve safer nanotechnology: design approaches and non-design approaches. Design approaches can be applied during the design stage for nanoparticles and products that incorporate nanoparticles. Non-design approaches are typically applied during subsequent stages in the product life cycle such as material processing, product manufacturing, product use, and product end-of-life. The non-design approaches are significantly important to increasing the safety of nanotechnology, and often incorporate the techniques and strategies from several disciplines including occupational hygiene, cleaner production, and product stewardship. For example, the use of inexpensive, low efficiency filters in recirculation systems has been shown to reduce nanoparticle concentration below levels found in a typical office within 20 min in a simulated nanomaterial production facility [7]. Non-design approaches include other examples such as the use of personal protective equipment, the use of less toxic solvents for purification steps, and the remote control of production.

The focus of this paper will be on the design approach to achieve safer nanotechnology. It is estimated that 70% of the costs of a product's development, manufacture and use is determined in the initial design of a product. Decisions made during the product design stage affect the impact of the product on both worker and consumer exposure and safety [8]. Therefore, it is prudent for companies to try to mitigate the potential risks of nanoparticles during the design stage rather than downstream during manufacturing or customer use.

So-called "Design for X" strategies are used to guide decisions during the product design stage to address particular design objectives. Several "Design for X" strategies have been developed and implemented by product manufacturers over the past several decades to address objectives such as manufacturing, assembly, testability, quality, reliability, and environmental. For example, the implementation of "Design for Manufacture" strategies has led to enormous benefits including simplification of products, reduction of manufacturing costs, improvement of quality, and reduction of time to market. "Design for Environment" is another strategy that has been used to address design issues associated with environmental health and safety over the full product life cycle [9]. These "Design for X" strategies are not mutually exclusive, and often several of these strategies are followed for a single product design.

The intent of this paper is to propose five design principles for product designers to use during the design stage for products that contain nanoparticles. These design principles will supplement Design for Environment strategies by addressing the unique properties of nanoparticles. These proposed design principles are largely untested and are offered as an initial framework that will require more testing, validation, and refinement. The term "product designers" is meant to include any member of a product design team including: design engineers, industrial designers, material scientists, and other team members. The objective is for product designers to design safer products that use nanoparticles by reducing the overall risk to human health and safety of the nanoparticle throughout the product life cycle. This would include consideration for degradation products or metabolites that may be generated during any point in the product life cycle.

The health and safety risk of the nanoparticle may be reduced by lowering the hazard and/or the exposure potential of the nanoparticle. The objective would be to move high risk nanoparticles to moderate or low risk situations. The ultimate goal of safer nanotechnology would be to move all nanoparticles incorporated into products to the low risk zone. A risk mitigation matrix is shown in Fig. 1 to illustrate this concept.

The type of nanoparticles used in products, as well as the manner in which they are incorporated into products is vastly diverse. Therefore, the guidelines to reduce the risks of nanoparticles must be general and practical enough to cover the wide spectrum of nanoparticles contained in products. There is no intended hierarchy for the five principles, since they are expected to cover a wide range of nanoparticles and product applications. The following are five general principles that product designers can use as an initial framework to address the risks of nanoparticles during the product design stage. These five principles could provide the initial foundation for a design approach termed "Design for Safer Nanotechnology" and are shown in Fig. 2.

2.1. S: size, surface, and structure. (Principle #1)

There are three major characteristics of nanoparticles (size, surface, and structure) that if changed, can affect fundamental nanoparticle properties such as color, conductivity, melting

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temperature, and reactivity. Further, changing any of these three characteristics may also alter the hazard and exposure potential of the nanoparticle. The objective for this design principle would be to change the size, surface, or structure of the nanoparticle so that the desired product functionality is preserved, but the hazard and/or exposure potential of the nanoparticle is diminished. The following is a brief description for each of the three characteristics.

2.1.1. Size

The size of a nanoparticle includes the dimensions for diameter, length, width, etc. which affects the fundamental properties of the nanoparticle. For example, the melting temperature for gold nanoparticles with a diameter of 2 nm is 650 K, while the melting temperature for gold particles with a diameter of 6 nm is 1150 K [10]. Also, research on the toxicity of nano titanium oxide has revealed there is a relationship between toxicity and particle size [11].

2.1.2. Surface

The surface characteristics affect the fundamental properties of the nanoparticle and include surface chemistry, surface charge, surface morphology, surface roughness, and surface contamination. For example, the greater the surface area per mass possessed by particles with the same chemistry, the greater the resultant biological (i.e. inflammatory or pro-oxidant) activity [12]. Further, oxidation of the surface of nanoparticles may influence their cytotoxic effects. The prolonged exposure to CdSe quantum dots to an oxidative environment can cause decomposition of the nanocrystal and release free cadmium from the quantum dot. Research has shown that the longer the oxidation time, the greater the cytotoxicity of the CdSe quantum dot [13].

2.1.3. Structure

The structure (crystal structure, shape, porosity, chemical composition, aggregation, etc.) of the nanoparticle can also affect the properties of the nanoparticle. For carbon nanotubes, structural differences include the wrapping angle (degree of twisting) of the lattice structure, or the presence of single or multi-walled nanotubes. From a product functionality standpoint, carbon nanotubes have been found to be either semiconducting or metallic based on minor variations of the wrapping angle of the nanotube [14]. Examples of different shapes of nanoparticles include spheres, cubes, tubes, fibers, cylinders, horns, and rings. Carbon nanotubes are cylindrical and fullerenes are spherical. Although both materials are comprised of covalently bonded carbon atoms, they exhibit many different fundamental properties. For example, research has found that carbon nanotubes have higher cytotoxicity to alveolar macrophage in vitro than fullerenes. The researchers state that “carbon materials with different geometric structures exhibit quite different cytotoxicity and bioactivity in vitro” [15]. Further, the structure of a nanoparticle also includes the degree that the nanoparticles are joined together by aggregation or agglomeration to form larger particles. For example, there are recent research results that indicate that the degree of agglomeration can affect the cytotoxicity of carbon nanotubes [16].

2.2. A: alternative materials (Principle #2)

This approach involves identifying an alternative material (nano or bulk), that can be used to replace the hazardous nanoparticle. The alternative material can be a drop in replacement, such as the use of soy based inks to replace petrochemical based inks for printing applications. Also, the hazardous nanoparticle could be replaced by a combination of alternative materials. For example, the lead heat stabilizers used for certain wire and cable products can be eliminated by instead using the synergistic materials of nanoclay and lead-free heat stabilizers [17,18]. The alternative material(s) should provide the desired functionality without the attendant toxicity issues. The use of alternative materials requires careful analysis, including the investigation of the potential effect the replacement may have on product functionality, hazards, and costs. There are several tools and methodologies available, such as P2Oasys [19] and Green Screen [20], to help product designers to assess the potential alternative materials.

If no alternative materials are available, then it may be necessary to eliminate the hazard by no longer using the nanoparticle in the product. This involves redesigning the product so that the functionality requirements that led to the initial choice of the hazardous nanoparticle is either significantly changed or eliminated. For example, brominated chemicals are hazardous materials that are added to the plastic enclosure of televisions to provide flame retardancy. A potential solution is to redesign the product such that the television power supply is properly shielded so that the plastic enclosure no longer needs to be flame retardant. Another option is to use other types of plastic resins that are inherently flame retardant and do not require the use of brominated chemical additives [21]. If a product is redesigned in this manner, it should still meet customer specifications and function as well as the initial product.

2.3. F: functionalization (Principle #3)

Functionalization is the intentional bonding of atoms or molecules to nanoparticles to change the properties of the nanoparticles. The objective for this design principle would be to functionalize the nanoparticle in a manner such that the desired product properties are preserved, but the hazard and/or exposure potential of the nanoparticle is reduced or eliminated. For example, CdSe nanocrystal quantum dots are often used as an alternative to fluorescent dyes for biological imaging and labeling. These CdSe quantum dots have been found to exhibit cytotoxicity [22]. Research results have indicated that the functionalization of nanocrystal quantum dots changes their physiochemical properties and reduces their cytotoxicity [23]. For biomedical applications, it is important to inhibit tissue accumulation of the nanoparticle, and instead promote the urinary excretion of the nanoparticle. This can be accomplished by increasing the solubility of the nanoparticle as well as preventing nanoparticle aggregation [24]. A recent study showed that covalently functionalized multi-walled carbon nanotubes exhibited rapid urinary clearance, as opposed to non-covalently functionalized multi-walled carbon nanotubes that accumulated in the liver [25].

2.4. E: encapsulation (Principle #4)

Encapsulation is a method used to completely enclose a nanoparticle within another material. The intent of this principle is to enclose a potentially hazardous nanoparticle within a material that is less hazardous. For example, two-photon photodynamic therapy (TP-PDT) is a cancer treatment method used to treat deeper diseases in vivo. However, the dyes used in this treatment are toxic and usually harm normal cells before they reach the target cancer cells. Research has shown that the potential toxicity of the dye can be circumvented by permanently encapsulating the dye within a bio-compatible nanoparticle polymer matrix. The matrix can prevent the dye from direct contact with cells, while at the same time the dyes are still capable of killing cancer cells efficiently when exposed to near infrared light [26]. However, the use of the encapsulation strategy should include certainty that the hazardous

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nanoparticle remains encapsulated during the relevant product life cycle stages where exposure may be an issue.

2.5. R: reduce the quantity (Principle #5)

There may be situations where applying the above design principles cannot reduce or eliminate the nanoparticle hazard while maintaining the desired product functionality. In these cases, the continued use of the hazardous nanoparticle may be necessary. If so, the design engineer should investigate the possibility of using smaller quantities of the hazardous nanoparticle in the product while maintaining product functionality. This principle has been applied by engineers in the lighting industry to significantly reduce over time the amount of the toxic mercury used in fluorescent lights. As a result, most compact fluorescent lamps now contain less than 5 mg of mercury [27].

3. Application of the Design for Safer Nanotechnology principles

Researchers at Brown University have identified physiochemical properties of inhaled fibers that affect biological activity and can be directly linked to the resultant toxicity of the fiber. The first property is fiber length, which can result in incomplete or frustrated phagocytosis by alveolar macrophages. The second property is redox activity that generates reactive oxygen species which can damage cellular lipids, proteins, and DNA. The third property is biopersistence that extends the duration of the fiber existence within the body and can lead to translocation to lung epithelial cells and pleura. These physiochemical properties have been shown to apply to asbestos fibers, and there is evidence that they may also apply to carbon nanotubes as well [28].

There are potential strategies to mitigate the adverse effects of these three physiochemical properties for carbon nanotubes. First, the length of the carbon nanotube could be restricted to a size that does not frustrate the phagocytosis process by alveolar macrophages. (Principle #1: Size). Second, the redox activity could potentially be reduced by removal of amorphous carbon and iron catalyst residues on the carbon nanotube surface. (Principle #1: Surface) Third, the biopersistence could possibly be decreased by functionalization of the carbon nanotube with groups imparting water dispersibility (e.g. carboxylate). (Principle #3: Functionalization) [28]. Further research is required to validate if these strategies will reduce the hazard and exposure potential for carbon nanotubes. This example illustrates the potential for applying the Design for Safer Nanotechnology principles.

4. Conclusions

Currently, there are many outstanding challenges that need to be addressed before product designers can fully apply these principles and make informed choices about nanoparticles. How should they characterize the nanoparticles used in their products? What are the key attributes that should be included in the characterization? How do the hazards found in nanoparticle research papers apply to the nanoparticles in their products? As the field of nanotechnology progresses, better answers to these questions will emerge.

Another major challenge is the lack of comprehensive data for the product performance, hazard, and exposure potential of nanoparticles with different shapes, sizes, surfaces, structures, and functionalization. These data gaps need to be addressed by further targeted research by government and industry. Since there are so many data gaps to be addressed, it would be impractical to cover all the combinations with research alone. Consequently, predictive models will also need to be developed to provide additional data. Ideally, this data will be housed in a centralized, open-access database available to researchers and industry.

Over time, the "Design for Safer Nanotechnology" principles could become more effective as additional performance, hazard, and exposure potential data are accumulated and made available. Ultimately, these initial design principles will need to be tested and refined over time to help guide product designers to make more informed and effective decisions for selecting the nanoparticles that they incorporate into their products.

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