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Review

Risk assessment of engineered nanomaterials and nanotechnologies—A review

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A B S T R A C T

With the increasing utilization of engineered nanomaterials (ENM), the potential exposure of workers to ENM is likely to increase significantly. Very little is known though, of the risks posed by ENM to human health, in particular concerning those characteristics that are technologically attractive: small size, high surface to mass ratio, and surface reactivity. ENM risk assessment is hampered by a lack of exposure as well as toxicity data specific to the multitude of ENM being developed. An economical approach to this problem urgently calls for intelligent testing strategies to capture essential features of ENM, thereby allowing over-arching ENM risk assessment. The data gaps of ENM risk assessment include (1) ENM aerosol standards and agreement on ENM key metrics; (2) dependable exposure scenarios, affordable monitoring technologies, exposure data and models; and (3) biomedical data on ENM translocation and toxicity, and associated testing strategies (which must be linked to the exposure scenarios). The special features of ENM do not, however, create a need to amend the current overall approach to the risk assessment of chemicals.

Contents

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1. Background

Feynman (1959) was one of the first to recognize the potential of nano-scale materials for our industrial society when he stated that there was “plenty of room at the bottom”. This quote stresses the possibilities of providing qualitatively new characteristics, e.g. to industrial processes or technological products. Today, engineered nanomaterials (ENM) have been defined as having at least one dimension ≤100 nm (Royal Society, 2004; Elder et al., 2009). They have attracted a great deal of attention during recent years due to their many technologically interesting properties (Adlakha-Hutcheon et al., 2009). The unique properties of ENM and their applications have given birth to large technological and economic growth and future expectations for industries using material at nano-scale. Nanotechnologies using ENM are envisaged to become the cornerstone for a number of industrial sectors such as micro-electronics, materials, paper, textile, energy, and cosmetics which are all capable of incorporating some of nano-scale-enabled properties into their goods (Adlakha-Hutcheon et al., 2009), with an estimated annual turnover of ENM-based products in the range of 1.1–2.5 trillion US dollars (Lux Research, 2006) by 2015. Nanotechnology applications will contribute positively to the quality of life through the production of light and durable materials, cleaner energy and inexpensive clean water production, as well as by enabling several beneficial medical applications, especially smart drugs (Maynard et al., 2006; Adlakha-Hutcheon et al., 2009). Additionally, great environmental benefits are predicted from nanotechnology-related applications because of the savings in raw materials, the consumption of natural resources and a reduced environmental pollution (Kuhlbusch et al., 2009; Nadagouda and Varma, 2009).

Today, ENM can be found in more than 800 consumer products (Woodrow Wilson International Centre for Scholars, http://nanotechproject.org) including electronic components, cosmetics, cigarette filters, antimicrobial and stain-resistant fabrics and sprays, sunscreens, cleaning products, ski waxes, different surfaces requiring antimicrobial properties in toilets, and self-cleaning windows (Woodrow Wilson International Centre for Scholars, http://nanotechproject.org; see also Elder et al., 2009). It should be noted, however, that some of the properties that make ENM so unique and beneficial for technological applications may also endanger human health through the potential induction of cyto- and genotoxic effects, inflammation and even cancer (Donaldson et al., 2005; Borm et al., 2006; Yang et al., 2009). These features include a large surface area to mass ratio, and associated increased surface reactivity, altered physico-chemical properties such as changes in melting point or solubility, electrical conductivity, or changes, e.g. in the crystalline structure of the materials (Maynard et al., 2004; Borm et al., 2006; Nel et al., 2006; Maynard and Aitken, 2007; Elder et al., 2009).

The association between toxic effects and dose is another issue awaiting resolution, a question very specific to ENM. Dose is linked to the “amount of material” involved in the exposure, a quantity which has in the past been linked typically and uniquely to “mass”. However, driven by the aerosol exposure route to nanoparticles, particle number and surface area have entered the discussion about the correct metric. Several investigators have provided evidence that ENM surface may in essence be the right ENM metrics for the dose definition, and dose so defined may have the best association with the effects resulting in a meaningful dose–effect curve (Oberdörster et al., 2005; Lindberg et al., 2009). This has stimulated research on ENM features and their correlation with toxic effects of ENM in order to assure safe use of nanotechnologies (Hoet et al., 2004; Maynard et al., 2004; Donaldson et al., 2005; Borm et al., 2006; Maynard and Aitken, 2007; Yang et al., 2009; Ostiguy et al., 2008). Furthermore, increasing attention has been focused on the nanotechnology–biology interface which is still poorly understood. At the same time, a responsible approach towards the development of ENM and nanotechnologies has been emphasized (Kuzma, 2007). Indeed, several organizations (SCENIHR, 2007) and countries (Raivio et al., 2008) have put emphasis on safety of nanotechnologies.

To complicate the issue of safety and risk assessment, ENM are not a uniform group of substances (Borm et al., 2006). To the contrary, they are characterized by a great diversity of substances and morphologies (Aitken et al., 2004; Maynard et al., 2004; Maynard and Aitken, 2007; Elder et al., 2009; Schulte et al., 2009). The remarkable diversity of ENM markedly complicates their risk assessment. There are currently about 50,000 different types of carbon nanotubes due to different raw materials, production processes and catalysts (Schulte et al., 2009), and the same diversity applies to many other types of ENM, rendering *ad hoc* risk assessment of all of these materials an immense task (Maynard et al., 2004).

2. Issues relevant to ENM risk assessment

Critical steps in the risk assessment of ENM remain so far the same as those used for the risk assessment of other types of chemicals, notably (1) hazard identification meaning identification of ENM properties that may cause hazards to health; (2) hazard characterization, which requires defining of dose-responses for critical target organ(s) and cell(s) and mechanisms of toxicity (Jia et al., 2005; Nel et al., 2006, 2009; Chou et al., 2008). Also the potential of different ENM to react with constituents of cells at the port of entry and beyond, i.e. lipids and proteins, should also assessed (Åkerman et al., 2002; Baroli et al., 2007; Balbus et al., 2007; Baciu et al., 2008; Elder et al., 2009). In order to evaluate the translocation or distribution of these materials in the body, one should also assess their capability to cross internal barriers such as blood–brain barrier, blood–placental barrier, blood–testicular barrier and many others (see Baroli et al., 2007; Cedervall et al., 2007a,b; Elder et al., 2009).

The next and third step in risk assessment is the assessment of exposure. ENM are produced from many substances, in many forms and sizes, and with a variety of surface coatings. The health risk assessment of such diverse materials requires validated analytical methods both for their characterization in bulk samples, and for their detection and measurement in workplace air. This is because ENM levels may be higher in occupational than in other environments, at least during certain operations; ENM are handled in large quantities in workplaces, and hence occupational settings carry the greatest potential for human exposure (see Maynard and Pui, 2007; Kuhlbusch et al., 2009; Peters et al., 2009). Risk assessment also requires an understanding of the transport processes between source and human receptor and how they modify the characteristics of the ENM (Seipenbusch et al., 2008). Airborne ENM (“aerosols”) can be characterized by measuring several metrics, especially number concentration, surface area and mass (SCENIHR, 2007; Ostiguy et al., 2008; Kuhlbusch et al., 2009; Peters et al., 2009).

These four steps in risk assessment—hazard identification, hazard characterization, exposure assessment, and risk characterization are ultimately combined in the risk assessment process. Risk assessment integrates the results of the four steps of the risk assessment process and aims at assessing the likelihood of occurrence of a given hazard in a certain exposure situation. The ultimate goal of current risk assessment paradigms is to be able to provide quantitative predictions of given risks enabling evidence-based risk management that is based on quantitative assessment of a given risk in a population. The various steps of risk assessment will be discussed in more detail below.