

Exposure assessment of engineered nanomaterials in the workplace

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Abstract—Nanotechnology is a rapidly growing field and numerous products containing engineered nanomaterials are already in the market. With the increasing use of engineered nanomaterials, it is expected to increase the exposures to nanomaterials in the workplace. However, the researches on the exposure assessment of nanomaterials to humans and the environment are just a beginning step, as the nanotechnology industries are expanding. Questionnaire surveys conducted by various organizations reveal that many nanotechnology companies are searching for information on exposure measurement for the protection of workers who handle nanomaterials. We analyze the trends of researches on the occupational exposure measurement of engineered nanomaterials and investigate the methodologies of exposure assessment recommended by the related working groups. This work is expected to fill the gaps in knowledge on the exposure assessment of nanomaterials.

Key words: Nanomaterials, Risk Assessment, Toxicity, Exposure Assessment, Workplace

INTRODUCTION

Nanotechnology, based on “small-scale science,” is a rapidly emerging and developing technology that has the potential for significant advances in various fields [1,2]. It deals with structures that are typically between 1 and 100 nm in size, and is considered with a considerable economic potential. The global manufacturing output of products containing nanomaterials is expected to rise to 2.6 trillion US\$ in 2015 [3]. However, some researchers have described nanotechnology as a two-edged sword. They are concerned that nanoparticles may enter and accumulate in the body, potentially causing harm or death to humans and, by extension, destroying the ecosystem. The safe use of nanotechnology may be the key issue for a great opportunity for the development of industry [4]. To use nanotechnology safely, it is essential to precisely control exposure to engineered nanomaterials during production or application processes, because workers can be directly exposed to nanomaterials for a long time. The questionnaire surveys conducted previously by the EU and USA show that many companies are finding measuring methods for the exposure to nanomaterials in workplace [5-8]. The exposure data are useful when making decisions in view of concerning risk management or evaluating the effectiveness of engineering controls and work practices to reducing worker exposures. Without workplace exposure data, it is difficult to accurately characterize the work environment, identify sources that are emitting nanomaterials, or estimate the amount of nanoparticle exposure that workers may receive [9]. Fig. 1 provides guidelines for implementing and documenting exposure assessment activities [10]. In this

review, we analyze the trends of researches on the occupational exposure measurement of engineered nanomaterials and provide the methodologies for the exposure assessment recommended by other related working groups.

TRENDS IN RESEARCH

1. International Organization

The Organization for Economic Cooperation and Development (OECD) and the International Standardization Organization (ISO) are in charge of standardizing the methods of measurement of nanomaterials in the workplace [3]. The OECD has several working groups (WG) to promote international co-operation that facilitates research, development, and responsible commercialization of nanotechnology in member countries and in non-member economies. Especially, the steering group 8 (SG8) is continuously updating reports on exposure measurement and mitigation [11]. The ISO Technical Committee (TC) 229 has established three WG to identify priority areas of standardization on nanotechnology. The WG-3 among groups is in charge of the health, safety and environmental aspects of nanotechnologies and has published a technical report titled “*Health and safety practices in occupational settings relevant to nanotechnologies*” which is a standard containing a guideline for characterizing nanoaerosol exposure [12].

2. USA

The National Institute for Occupational Safety and Health (NIOSH) is the leading US agency conducting research and providing guidance on the occupational safety and health implications and applications of nanotechnology [13]. In addition, the Environmental Protection Agency (EPA) plays a leading role in developing environmental applications for nanotechnology [14]. In 2007, the EPA pub-

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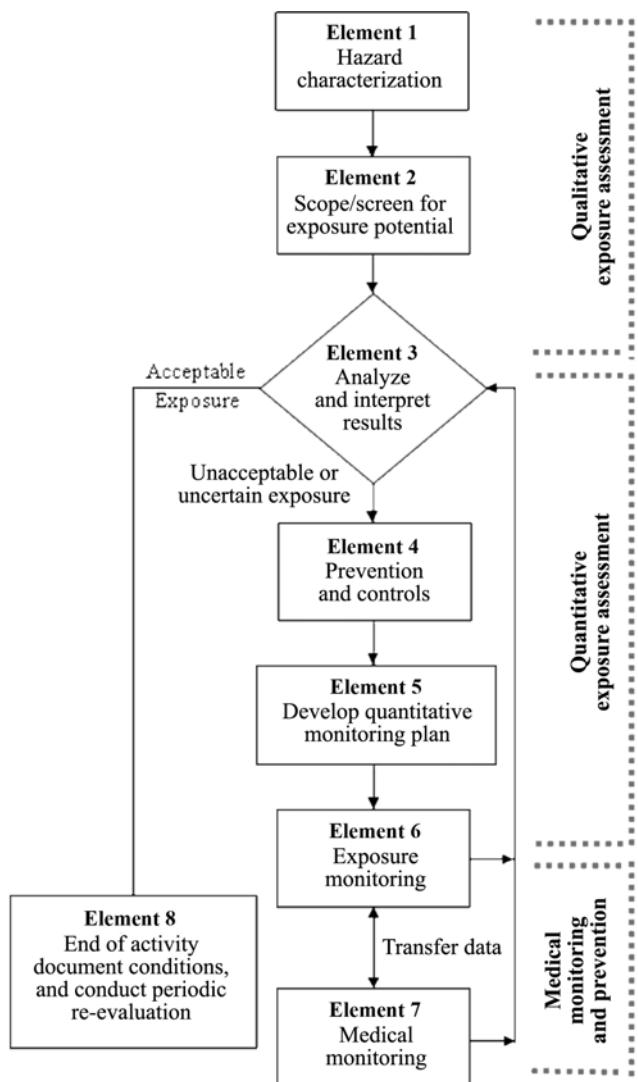


Fig. 1. Overview of the exposure assessment strategy [9].

lished a “Nanotechnology white paper” to address any potential risks due to the environmental exposure to nanomaterials. This report also notes the occupational exposure measurement to nanomaterials.

The researches on the potentially harmful effects by nanomaterials are being led by not only federal agencies but also companies and other organizations interested in this subject. The project on Emerging Nanotechnologies is progressing with a partnership between the Woodrow Wilson International Center and the Pew Charitable Trusts in order to inform the debate and to draw an active public and policy dialogue [15]. In 2005, DuPont and the Environmental Defense entered into a partnership to develop the Nano Risk Framework for the responsible development, production, use, and end-of-life disposal or recycling of engineered nanomaterials [16]. To define what would be best practice to protect workers with respect to handling engineered nanoparticles, the Nanoparticle Occupational Safety and Health (NOSH) Consortium was formed in 2005 with 16 full and strategic members, including DuPont, Intel Corporation, Boeing, Degussa, GE, Kimberly-Clark, Department of Energy Office of Science (US), NIOSH(US), Health and Safety Executive (UK), etc. [1].

3. Europe

In the United Kingdom, the Royal Academy of Engineering and the Royal Society have established a working group to consider the potential health risks arising from the development of nanotechnology in general. The Health and Safety Executive (HSE) is leading groups on the occupational hygiene implications of the manufacture of nanomaterials. The HSE supports the research of the Health and Safety Laboratory (HSL), an agency of the HSE, and other project groups to protect workers' health and safety in the workplace from exposure to nanomaterials [17]. The Federal Institute for Occupational Safety and Health (BAuA, Bundesanstalt für Arbeitsschutz und Arbeitsmedizin) plays a key role in designing a safe, healthy and competitive workplace of Germany in collaboration with the German Chemical Industry Association (VCI, Verband der Chemischen Industrie) [18]. The German Federal Ministry of Education and Research (BMBF, Bundesministerium für Bildung und Forschung) and industrial partners, such as Bayer, BASF, Degussa etc., support the NANOCARE research project, which focuses on the possible impact of nanomaterials on humans in the workplace [19]. In Switzerland, the Federal Office for the Environment (FOEN) and the Swiss Federal Office of Public Health (SFOPH) investigate the potential risks of engineered nanoparticles [3]. Research for evaluation and control of occupational health risks from nanoparticles in Nordic countries consisting of Denmark, Finland, Iceland, Norway and Sweden was performed by the Nordic Council. Especially, Denmark focuses on study of the exposure to nanoparticles used at the paint and lacquer industry and nanoparticle-base pump and spray products [20]. The European projects on controlling and monitoring of engineered nanomaterials exposure in workplace are arranged in Table 1.

4. Asian Countries

In Japan, the National Institute of Advanced Industrial Science and Technology (AIST) published risk assessment reports on three representative manufactured nanomaterials, C_{60} , carbon nanotubes and TiO_2 through the project “Research and Development of Nanoparticle Characterization Methods” of the New Energy and Industrial Technology Development Organization (NEDO) [22]. The National Institute of Occupational Safety and Health Japan (NIOSH) has had a project on possible health issues due to exposure to manufactured nanomaterials in the workplace since 2007 [23].

In China, the National Center for NanoSciences and Technology (NCNST), the Institute of High Energy Physics (IHEP) and Chinese Academy of Sciences (CAS) built the co-working laboratory for the Bio-Environmental Effects of Nanomaterials & Nanosafety in 2006. This lab studies a standard procedure for safety assessment of nanoproducts for nano-industries/enterprises including assessment methods, and identifying the toxicity classes of nanomaterials [24].

5. Korea

The Korean government established the “National Strategic Nanotechnology Development Plan” in 2001. According to the Phase-2 Korea National Nanotechnology Development Plan, the Korean government has programs on human health and environmental safety issues of nanotechnologies. The Ministry of Environment (MOE) has been conducting the “Ecotopia-21 project” since 2001 to promote the development of environmental technologies. The final goal of the research plans is to support the establishment of infrastructure necessary to minimize potential risks derived from the manu-

Table 1. Recent and on-going projects of Europe on nanomaterials exposure in the workplace

Country	Project	Principal Investigator (Institution)	Period	Total Funding (Funding Source)
EU	Safe production and use of nanomaterials (NANOSAFE 2)	F. Schuster (CES)	2005-2009	\$10,758,238 (DG Research)
	The behavior of aerosols released to ambient air from nanoparticle manufacturing- A pre-normative study (Nanotransport)	Q. Wu (Det Norske Veritas AS Hoevik, Norway)	2006-2007	\$691,617 (DG Research)
	Inflammatory and genotoxic effects of engineered nanomaterials (NANOSH)	K. Savolainen (Finnish Institute of Occupational Health)	2006-2009	\$3,688,625 (DG Research)
UK	The Assessment of Different Metrics of the Concentration of Nano (Ultrafine) Particles in Existing and New Industries	C. Elliot-Minty (HSE)	2002-2004	\$195,744 (HSE)
	Nanoparticles: An occupational hygiene review	R. Aitken (Institute of Occupational Medicine)	2004	\$30,247 (HSE)
	HSL Investment Research Programme (Nanochallenge)	N/A	2007-2010	\$1,814,814 (HSL/HSE)
Germany	Research project to study the safe handling of nanomaterials	H. Krug (Forschungszentrum Karlsruhe)	2006-2009	\$7,684,635 (BMBF)
Switzerland	Manufactured nanoparticles in Swiss industries and the potential for human exposures (Nanoinventory)	M. Riediker (Institute of Occupational Health Sciences, Switzerland)	2005-2008	\$278,683 (Swiss and French authority)
	How to assess the adequacy of safety measures for manufactured nanoparticles	M. Riediker	2006-2010	N/A
	Use of nanoparticles in industry: safety aspects (NanoWorkRisk)	M. Riediker	2007-2010	\$167,202
Denmark	Evaluation and control of occupational health risks from nanoparticles	T. Schneider (National Research Centre for the Working Environment Denmark)	2006-2007	\$61,938 (Nordic Council of Ministers)
	Nanoparticles in the paint- and lacquer industry. Exposure and toxic properties (NANOKEIM)	U. Vogel (National Research Centre for the Working Environment Denmark)	2007-2010	\$2,065,762 (The Danish Working Environment Research Fund)
	Nano-technological materials and products in the plastics industry: Exposure assessment and toxicological properties (NANOPLAST)	P. A. Clausen (National Research Centre for the Working Environment Denmark)	2007-2010	\$1,045,110 (Danish Working Environment Research Fund)
Finland	Nanosafety in Finland	M. Hjelt (Gaia Consulting Ltd)	2007-2008	\$67,625
Greece	Technology development for optimizing air quality in industrial buildings		2003-2007	\$1,126,414

facture, distribution and disposal of nanomaterials and consumer products containing nanomaterials [21].

Interestingly, the governmental agencies constitute a consortium in cooperation with nanotechnology companies to support research on risk assessment of nanomaterials in the workplace in the US and Europe, while Asian countries such as Korea, Japan, and China operate a central control on risk assessment through only governmental agencies. In addition, Asian countries do not have a strong network to share common strategies on the risk assessment in the workplace compared to the EU. The Asian countries have shown a willingness

to establish a strong network. However, this willingness has not been made yet. Currently, Asian countries are conducting researches independently. This situation is due to the lack of funds and human resources for research on the risk assessment of nanotechnology. For this reason, Asian countries are behind Europe and the US in risk management of nanomaterials in workplace [25].

MEASURING METHODOLOGY

Although many organizations in the world have researched vari-

Table 2. Potential sources of occupational exposure for various synthesis processes [14]

Synthesis process	Particle formation	Exposure source or worker activity	Primary exposure route
Gas phase	In air	Direct leakage from reactor, especially if the reactor is operated at positive pressure	Inhalation
		Product recovery from bag filters in reactors	Inhalation/Dermal
		Processing and packaging of dry powder	Inhalation/Dermal
		Equipment cleaning/maintenance (including reactor evacuation and spent filters)	Dermal (and Inhalation during reactor evacuation)
Vapor deposition	On substrate	Product recovery from reactor/Dry contamination of workplace	Inhalation
		Processing and packaging of dry powder	Inhalation/Dermal
		Equipment cleaning/maintenance (including reactor evacuation)	Dermal (and Inhalation during reactor evacuation)
Colloidal/Attrition	Liquid suspension	If liquid suspension is processed into a powder, potential exposure during spray drying to create a powder, and the processing and packaging of the dry powder	Inhalation/Dermal
		Equipment cleaning/maintenance	Dermal

ous methods for the exposure assessment of nanomaterials in the workplace, a standard or an agreeable methodology with each other has not been established yet. The main reason is the difficulty in precise analysis of airborne nanomaterials in the workplace, because nanomaterials have unique physicochemical properties different from those of bulk materials. Currently, the measuring methodology recommended by research organizations mostly is a modified form of conventional measuring methods for micro-sized materials. It can be summarized as follows.

1. Classification of Production Processes

First, the measurement of nanomaterials in the workplace should be done in the production process. Most synthesis methods of nanoparticles in the gas phase are based on homogeneous nucleation of a supersaturated vapor and subsequent particle growth by condensation and coagulation. The methods can be categorized by the heating or evaporation process used [26]. These include flame pyrolysis, furnace flow reactors, laser induced pyrolysis, laser vaporization, thermal plasma, microwave plasma, sputtering, laser ablation, droplet evaporation. Gas phase synthesis methods are generally considered to offer easy bench-up from lab-scale to industrial level processes. In the gaseous phase reaction, primary particles produced individually very rapidly form secondary larger ones.

To prevent this phenomenon, nanomaterials are produced through reaction in solution, by adding stabilizing agents (e.g., surfactant). Nanoparticles produced by wet chemical methods, namely, sol-gel chemistry, may also be collected by filtering or by spray drying to produce a dry powder. The production process using liquid media decreases the exposure possibility by inhalation [27]. The mechanical attrition methods are contrastive to the previous methods where nanoparticles were built by “bottom-up method” from individual molecules; in attrition methods nanoparticles are produced by top-down method from larger particles. Size reduction by grinding and milling is a very well established industrial process used to produce progressively finer forms of materials including minerals such as

clay, coal and metals [17]. In all nanoparticles production processes, there are potential risks for exposure, as summarized in Table 2. However, the Maynard group suggested the risk of particle release during production may be low because of appropriate filtering systems [28]. Exposure to workers is more likely to happen during handling and bagging of the material.

2. Measuring Equipment

Various devices are used to analyze the particulate concentration by mass, surface or number of particles in suspension in a liquid or gaseous medium and sampling. Table 3 briefly illustrates some of these devices and their range of applicability [29].

3. Baseline Assessment

Measuring events should be carried out before starting of processes in order to ensure an adequate baseline against which to assess potential increases in airborne concentrations that result from nanoparticle handling. Air monitoring data, in particular, should be collected to establish pre-manufacture mass and particle number concentrations, and then again after operations have commenced. The data should include short term exposure levels, maximal measured concentrations, and eight-hour time-weighted averages for workers with the highest potential exposures [16].

4. Personal and Area Sampling

Assessments to determine worker exposures to nanomaterials can be performed by using industrial hygiene sampling method: area and personal sampling. An area sample collected at a fixed point in the workplace reflects physicochemical characteristics of airborne nanomaterials present at that point. Results from area sampling should be analyzed with caution because they do not represent employees' actual exposures to nanomaterials. To compensate for this drawback, personal sampling is conducted in the breathing zone, a hemisphere forward of the shoulders with a radius of approximately 6 to 9 inches, of an individual using a personal air pump. The sampling device is directly attached to the worker and worn continuously during all work and rest operations [10]. Some exam-

Table 3. Instruments and techniques for monitoring nanoaerosol exposure [29]

Metric	Devices		Remarks
Mass	TEOM (Tapered Element Oscillating Microbalance)	0.030-10 μm	Not size selective. Pre-separator is needed. Measures mass concentration of PM. Measures only nonvolatile components of PM.
Number	ELPI (Electrical Low Pressure Impactor)	0.030-10 μm	Size distribution with time resolution from 2-15 s (aerodynamic dia.). Low pressure may cause volatile particles to evaporate.
	CPC (Condensation Particle Counter)	10 nm <	Not size selective. Pre-separator is needed. Diffusion screen to limit top size to 1 μm .
	SMPS (Scanning Mobility Particle Sizer)	0.01-0.7 μm	Pre-separator must be used to remove particles larger than 1.0 μm for aerosol measurements. Measure number concentration (mobility diameter).
	Nano-SMPS	3-50 nm	Time resolution of about 10 s required to scan all intervals. Not fully characterized and developed.
	EAA (Electrical Aerosol Analyzer)	0.003-1.0 μm	Pre-separator must be used to remove particles larger than 1.0 μm for aerosol measurements. Measure number concentration (mobility diameter).
	APS (Aerodynamic Particle Sizer)	0.453-20 μm	Time-of-flight aerodynamic sizing accounts.
	Diffusion battery	0.01-0.5 μm	Measure number concentration (aerodynamic dia.).
Surface area	DC (Diffusion Charger)	<100 nm	Pre-separator must be used to remove particles larger than 1.0 μm for aerosol measurements. Measure active surface area (for below 100 nm particles).
	Epiphaniometer	<7.0 μm	Measures Fuchi surface area. Time resolution is between 5-30 min depending upon the analysis code used. Bulky, complex, and costly.
	PAS (Photoelectrical Aerosol Sensor)	<1 μm	Pre-separator must be used to remove particles larger than 1.0 μm for aerosol measurements.
Composition	ATOFMS	0.3-50 μm	Aerodynamic diameter and chemical composition. Real-time measurement of up to 600 part/min.
Sampling	Cascade impactor	PM2.5 (PM10)	An instrument for the classification of aerosols (Aerodynamic dia.). A series of orifices of decreasing size; the air flow is normal to collecting surfaces on which aerosols are collected by inertial impaction.
	LPI (Low Pressure Impactor)	0.030-10 μm	An instrument for the classification of aerosols (Aerodynamic dia.). A low pressure impactor is an impaction device to separate airborne particles at low pressure condition.
	MOUDI (Micro-Orifice Uniform Deposit Impactor)	0.056-10 μm	An instrument for the classification of aerosols (Aerodynamic dia.). Not real-time, gravimetric and chemical analysis performed after collection.
	Nano-MOUDI	0.010-18 μm	Low pressure may cause volatile particles to evaporate.
	ESP (Electrostatic precipitator)	<1.0 μm	An instrument for the classification of aerosols (mobility dia.). The particulate collection device that removes particles from a flowing gas (such as air) using the force of an induced electrostatic charge.

plexes including the measurement of carbon nanofiber and quantum dot were reported by the NIOSH research team. They conducted exposure assessment at a research facility to determine whether fugitive emissions occurred during laboratory processes. Task-based air and surface sampling was conducted using a vacuum method. Real-time aerosol measurement was conducted by CPC, SMPS and ELPI. In addition, air and surface samples were collected by NIOSH Method 5040 for subsequent total carbon analysis, as were air samples for analysis by TEM [30]. Another field survey was conducted at a R&D laboratory to determine whether quantum dots (2-8 nm) were released during various processes. Surface samples

were collected using Ghostwipe® substrates and air samples were collected on mixed cellulose ester (MCE) filters. Airborne particle concentrations were measured by CPC in the work areas [13]. Currently, there are few published papers which show the sampling and monitoring data of engineered nanomaterials in field. Most research groups conducted exposure assessment under controlled conditions in the laboratory [31,32]. These results may be helpful to understand mobility of airborne nanomaterials emitted in the process. However, it has a gap in exposure feature between produced nanomaterials in laboratory and generated nanomaterials under production process in the fields. More monitoring data in the field including

various variables, such as vent facility and reactor volume etc., are needed to establish the methodology of exposure assessment. Therefore, the research by cooperation with nanotechnology companies is essential to accurate exposure assessment in the workplace.

5. Biological Monitoring

Biomonitoring, which is used to detect the level of nanoparticles in accessible biological fluids, such as blood or urine, could be a means of determining whether and to what extent exposures have occurred [33]. However, given the current limited knowledge on nanomaterials in commerce, their uses, and their fate in the environment and in the human body, it is difficult to identify nanomaterials for biomonitoring. Should biomonitoring become more feasible in the future, it presents an opportunity to assess the spatial and temporal distribution of nanomaterials in workers and the general population.

6. Worker Health Monitoring and Medical Surveillance

In the context of workplace exposures to low concentrations of nanomaterials, health surveillance in the form of measuring changes in biological indicators from baseline levels can be used as an indicator of whether exposure is occurring. There are two strategies for health monitoring. One strategy is to find early identifiable intermediate biological markers (such as markers of pulmonary inflammation) that might indicate disease risk. Another approach to assess the effectiveness of controls is the assessment of the medical history of nanotechnology workers to identify increased frequency of sentinel health problems that might be linked to exposure to nanoparticles [33]. The exposure data linked with medical data reduces the uncertainty about whether exposures are appropriately controlled. It also provides direction for worker health counseling and training for controlling exposures and mitigating hazards [10].

PROSPECTIVES

In this review, a variety of efforts on occupational hygiene investigations have been presented, concentrating on the methodology of exposure assessment of engineered nanomaterials. With a developing nanotechnology industry, any possible problems on occupational hygiene in the nanotechnology workplace are actively discussed in the USA and EU, because of their partnership with nanotechnology industries and strong network for discussion and communication on risk assessment. In spite of their efforts, there are currently no international standard methods for measuring engineered nanomaterials [30]. The first step for risk assessment of nanomaterials in workplace is to analyze characters, such as number, mass concentration and surface area etc., of nanomaterials emitted in production or application process using monitoring and sampling methods. Currently, methodologies for measurement of nanomaterials recommended by most organizations are not largely different from conventional ones for the measurement of micro-sized materials. Importantly, it is a key point whether equipment can precisely and accurately measure nano-sized materials. SMPS is suggested as the most appropriate monitoring equipment due to the possible measurement of a full sized distribution in a short period of time [17,29]. However, there are doubts on the reliability of SMPS; for instance, this equipment cannot distinguish natural nanomaterials from engineered nanomaterials. Many research groups, including our groups, try to confirm the reliability of SMPS through lab-based study and

field monitoring. In the long run, smart sensors might detect dangerous exposure levels of nanomaterials in the workplace. To achieve this objective, not only the development of portable, cost-effective and easy in use measuring equipment but also research on the behavior of nanomaterials in the body, including dose, transport, clearance, accumulation, transformation and response should be progressing. Based on exposure assessment data, the exposure standard of nanomaterials in the workplace would be established. Under this standard, development of personal protective equipment and process control would be conducted to prevent exposure to nanomaterials. Consequently, by global research on exposure assessment, the advent of safe nanotechnologies will be advanced.

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