J Nanopart Res (2009) 11:1651–1659
DOI 10.1007/s11051-009-9703-1

SPECIAL ISSUE: ENVIRONMENTAL AND HUMAN EXPOSURE OF NANOMATERIALS

Distinguishing nanomaterial particles from background airborne particulate matter for quantitative exposure assessment

Mariko Ono-Ogasawara · Fumio Serita · Mitsutoshi Takaya

Received: 27 January 2009 / Accepted: 1 July 2009 / Published online: 22 July 2009

Abstract As the production of engineered nanomaterials quantitatively expands, the chance that workers involved in the manufacturing process will be exposed to nanoparticles also increases. A risk management system is needed for workplaces in the nanomaterial industry based on the precautionary principle. One of the problems in the risk management system is difficulty of exposure assessment. In this article, examples of exposure assessment in nanomaterial industries are reviewed with a focus on distinguishing engineered nanomaterial particles from background nanoparticles in workplace atmosphere. An approach by JNIOSH (Japan National Institute of Occupational Safety and Health) to quantitatively measure exposure to carbonaceous nanomaterials is also introduced. In addition to real-time measurements and qualitative analysis by electron microscopy, quantitative chemical analysis is necessary for quantitatively assessing exposure to nanomaterials. Chemical analysis is suitable for quantitative exposure measurement especially at facilities with high levels of background NPs.

Keywords Nanomaterial · Nanoparticle · Exposure assessment · Fullerene · EHS · Carbon nanotube · Multi-walled carbon nanotube

M. Ono-Ogasawara (✉) · F. Serita · M. Takaya
Japan National Institute of Occupational Safety and Health, 6-21-1 Nagao, Tama, Kawasaki 214-8585, Japan
e-mail: ono@h.jniosh.go.jp

Introduction

As the production of engineered nanomaterials (NMs) quantitatively expands, the chance that workers involved in the manufacturing process will be exposed to nanoparticles (NPs) also increases. Since some studies have found NPs to have greater biological activity than larger particles of the same material (Grassian et al. 2007; Obersdörster 1996), and potential toxicity has been observed in laboratory animals exposed to some types of carbon nanotubes (CNTs) (Lam et al. 2004; Shvedova et al. 2005, 2008a, b; Takagi et al. 2008; Poland et al. 2008, Warheit et al. 2004), a risk management system is needed for workplaces involved in NM production and handling according to the precautionary principle (Paik et al. 2008; Schulte et al. 2008). Guidelines for handling NMs have been issued in several countries (BauA 2008; NIOSH 2008; BSI 2008a, b; IRSST 2009).

One of the key problems for such a risk management system is exposure assessment. Metrics for exposure assessment have not yet been determined since the mechanism by which NMs affect health is still under investigation. Surface area is recommended as a better metric than mass concentration (Obersdörster 1996, 2001; Donaldson et al. 1998) for some rodent studies. Another problem for assessing NM particle exposure is high concentrations of background NPs in ambient and workplace air from fossil fuel combustion, secondary generation in the

atmosphere and other work processes. Although various instruments can measure the number, size, mass and surface area of NPs in real time, these real-time measurements are not selective for different kinds of NPs. As a result, background NPs can interfere with quantitative exposure assessments.

Although a metric related to the adverse health effects of NPs has not yet been determined, when engineering controls are instituted in production and handling of NMs, some metric is necessary for monitoring the workplace environment quantitatively and evaluating the effectiveness of the engineering controls. For quantitative analysis, it is necessary to distinguish the engineered NPs from background NPs. In this article, examples of measurement methods used in the NM industry were reviewed with a focus on distinguishing NM particles from background NPs to quantitatively measure NMs. Examples of JNIOSH methods are also introduced, and an approach to quantitative exposure assessment is discussed.

Real-time measurement instruments and analytical methods for nanomaterials

The various types of real-time instruments that are used to monitor NPs in the workplace are summarized in guidance documents (HSE 2006; ISO 2008). Instruments that are available in the workplace are listed in Table 1. Instruments for the detection of micron-sized particles are included in this list because particles of this size can be formed by agglomeration/aggregation of NPs. The details of these instruments were obtained from publications relating to particle monitoring.

The size and number of particles are monitored simultaneously with a Scanning Mobility Particle Sizer (SMPS^{TM}) and an Electrical Low Pressure Impactor (ELPI). Measurements with these instruments are based on different physical principles, and as a result, these instruments could be having different responses even if the same type of particle is monitored. They are not suitable for measurement in workplace including personal monitoring because of their weight (>20 kg) and size. The time resolution of SMPS is not sufficient for monitoring the sudden generation of NPs.

Total particle number is monitored with portable instruments such as a Condensation Particle Counter (CPC) and an Optical Particle Counter (OPC) for nano-sized and micron-size particles, respectively. These instruments detect particles via a light-scattering method and continuously measure the total number of particles in a certain size range. The time resolutions of these instruments range from one to a few seconds. These instruments are very useful for assessing emissions and measuring the particle exposure of nearby worker due to their light weight and quick response. Usually CPC, which is used as a detector in SMPS, uses *n*-butanol or iso-propanol to increase the size of particles by condensation to detect the particles by light scattering. Use of these instruments is restricted to certain selected facilities, since they release small amounts of organic vapor into the environment.

Surface area is considered to be an important metric for exposure assessment since it is associated with biological effects in rodent studies. A Diffusion Charger (DC) is a real-time surface area monitor, which mainly responds to particles smaller than about

Table 1 Typical real-time measurement instruments for nano- to micron-size particles in workplace

Metrics	Range*	Name	Portability
Number	5–1000 nm	Scanning Mobility Particle Sizer (SMPS)**	Not portable
Number–Size distribution	7–10000 nm	Electrical Low Pressure Impactor (ELPI)	Not portable
Total number	10–1000 nm	Condensation Particle Counter (CPC)***	Portable (handheld)
	300–5000 nm	Optical particle Counter (OPC)	Portable (handheld)
Surface area	<100 nm	Diffusion Charger-based Surface-Area Monitor (DC)	Portable (ca. 7 kg)
Mass		Tapered Element Oscillating Monitor (TEOM)	Not portable

* Ranges of detectable size of particles could be different for model of instruments

** Same as Differential Mobility Analyzer (DMA)

*** Same as Condensation Nucleus Counter (CNC)

100 nm. The data of DC are used for calculating the surface area of particles deposited on the trachea or alveoli (Shin et al. 2007).

The mass concentration of particles has been used as a metric for evaluating work environments. Although the contribution of nano-sized particles to the total mass concentration of particles is not large, the mass of respirable particles is important. Continuous measurement of mass concentration can be conducted with a Tapered Element Oscillating Monitor (TEOM). Off-line and integrated measurements are conducted gravimetrically by filter sampling. The mass size distribution of nano- to micron-sized particles is determined by ELPI and Micro Orifice Uniform Deposit Impactor (MOUDI).

Both Scanning Electron Microscopy (SEM) and Transmission Electron Microscopy (TEM) are important tools for identifying particles by size and morphology. EM combined with Energy Dispersive X-ray Spectroscopy (EDX) can chemically assign each particle. However, EM is a qualitative analytical method, and the particles observed by EM may not be representative.

For quantitative analysis of NM particles, chemical analysis is also used to determine bulk materials. When the bulk element of NPs is a metal, Inductively Coupled Plasma/Mass Spectrometry (ICP/MS) is used because of its high sensitivity if particles are dissolved into an appropriate solvent for chemical analysis. Although the sensitivity for carbonaceous NMs is usually lower than that for metals, chemical analysis can be used to determine these NMs. High-performance liquid chromatography with ultraviolet detection (HPLC/UV) can be used for monitoring exposure to fullerenes. HPLC is usually used for purification of fullerenes in production as well as for determination in biological samples (Xia et al. 2006) and in geologic materials (Heymann et al. 1995). Carbonaceous aerosols in the workplace and ambient environments have been monitored by carbon analysis to evaluate the contribution of different emission sources. For example, elemental carbon (EC), which mainly consists of graphite-like carbon, is recognized as an index of diesel engine exhaust (National Institute for Occupational Safety and Health 1994). There are various methods and instruments for carbon analysis, such as thermal/optical (Birch and Cary 1996; Chow et al. 1993), thermal/chemical (Petzpd and Niessner 1996) and continuous optical (e.g., Aethelometer; Hansen et al. 1984) methods. These methods can be applied to exposure assessments of carbonaceous NMs.

Field survey of NPs in non-nanomaterial workplaces

In addition to the production of engineered NPs, other emission sources of NPs in the workplace include combustion of fossil fuels and condensation of metal vapors emitted during welding, soldering, and smelting. Even mechanical processes can generate ultrafine particles less than 100 nm through the grinding of various substrates (Zimmer and Biswas 2001) and beryllium ceramics (McCawley et al. 2001).

For welding processes, the spatial distribution of NPs was determined by CPC measurements (Zimmer 2002). Number size distributions were compared with TEM observations to establish the relationship between size, morphology, and the results of real-time measurements. For simulated welding operations, particles having different morphologies showed different size distributions as measured by SMPS and CPC (Brouwer et al. 2004). In this study, surface area measurements by the Brunauer–Emmet–Teller method and SEM analysis were conducted for samples collected by ELPI. Mass size distributions near various types of welding operations were measured gravimetrically for samples collected by MOUDI (Dasch and D'Arcy 2008). SEM observations and elemental analysis revealed useful additional information for exposure assessment.

In a primary aluminum smelter, SMPS detection found that the generation of particles less than 50 nm was the highest in the process of anode changing (Thomassen et al. 2006). These were not observed by TEM since the particles were produced by condensation of vapors and lost during sampling or in the high-vacuum conditions of TEM.

A series of measurements was conducted in automobile-related facilities (Peters et al. 2006; Heitbrink et al. 2007, 2009; Evans et al. 2008). The spatial distribution of hot spots of fine and ultrafine particle emissions relating to work processes was visualized with data obtained by CPC and OPC. The spatial map of number concentration showed that NPs were mainly emitted from direct-fire heaters, not from the work process itself. They concluded that filter-based mass concentration was not a good

indicator of ultrafine particles because particle counts were not related to mass concentration.

Field survey of NPs in nanomaterial workplaces

Methods of distinguishing engineering NM particles from background particulate matter are reviewed in this section. NP measurements can be affected by particles from ambient air, production facilities, and impurities/by-products from the production process.

Metal oxides

A pilot-scale facility for the production of metal oxide NPs using a high-temperature gas-phase process was monitored by CPC and SMPS (Demou et al. 2008). The observed number concentrations were well explained by the process used at the facility. However, the mass concentration did not correlate well with the process.

Estimated respirable mass concentrations calculated from CPC and OPC data (Peters et al. 2006) were used at a lithium titanate NP production facility (Peters et al. 2009). The estimated mass concentrations correlated well with workplace operation. On the other hand, number concentrations did not. In this case, SEM and TEM analyses including elemental analysis can evaluate the origin of particles based on morphology and composition. Possible contaminants in this facility were welding fumes, particles from grinding, and particles from outside the facility.

Carbon black

Carbon black is widely used in industries such as the paint, printing, and rubber industries. The size of the primary particles of carbon black is less than 100 nm. Several primary particles usually connect to produce micron-sized secondary particles often having a branched structure. The expected size of particles in carbon black facilities ranges from 20–30 nm to a few micrometers. The bagging, pelletizing, and reactor areas of a carbon black manufacturing facility were assessed with CPC and SMPS, and the sizes of the NPs were classified as PM_{10}, $PM_{2.5}$, and PM_1 (Kuhlbusch et al. 2004, 2006). In addition, continuous measurements of mass and carbon were conducted using TEOM and an Aethalometer, respectively, since carbon, especially EC, is an index of carbon black. The ratios of SMPS data for inside/outside the factory and with/without work showed that the size distribution changed during work processes. The ratios of EC to $PM_{2.5}$ and PM_1 particles were high, and a peak of a specific size in the number size distribution was observed. Therefore, it is possible that carbon blacks of micron size were emitted into the workplace air. Particles of approximately 400 nm and 8 μm as well as particles of approximately 100 nm were generated in the bag filling and reactor areas (i.e., a leak occurred), respectively. Particles of 30–50 nm were generated from forklift engines and road traffic near the factory. Although EC is also an index of diesel exhaust particles, the EC ratio inside/outside the factory or the EC ratio with/without work are possibly supporting metrics.

Carbon nanotubes and nanofibers

A multi-wall carbon nanotube (MWCNT) laboratory was surveyed with SMPS and an Aethalometer, and the mass of collected total particles was measured (Han et al. 2008). The total number concentrations calculated from SMPS data responded to oil pump operation more strongly (>30,000 particles/cm^3) than CNT release (ca. 2,000 particles/cm^3). On the other hand, the Aethalometer responded only to CNT release. In a laboratory without an EC source such as this, EC is a possible metric for CNT exposure. For quantitative analysis, it is necessary to determine the response factor of CNTs in analyses using an Aethalometer. Han et al. counted MWCNT fibers with aspect ratios larger than 3:1 after the fibers were distinguished from asbestos by SEM/EDX analysis. Engineering control was evaluated by this combined method. MWCNT aerosols generated for an inhalation study were monitored by a thermal/optical instrument (Myojo et al. 2008). In this method, the temperature of the final stage of the analytical protocol for carbon analysis (National Institute for Occupational Safety and 1994) was 920 °C. They compared thermograms of MWCNT to those of the standard material for diesel forklift exhaust (NIST SRM 2975). As the outputs of the detector during the final stage are very different, such output is expected to be an index of MWCNTs. Optical correction was not used in this study since no pyrolyzed carbon was observed for this MWCNT.

In JNIOSH field monitoring of MWCNTs, we used a thermal/optical instrument with a modified IMPROVE protocol (Chow et al. 1993). The final temperature of carbon analysis was 920 °C. The carbon evolved at 920 °C with oxygen is specific to MWCNT (Sigma-Aldrich, 659258, diameter = 110–170 nm, length = 5–9 μm) as shown in Fig. 1a and is associated with the concentration of the MWCNT aerosol. In this case, the optical correction was not used because only the carbon evolved at 920 °C is monitored. On the other hand, thermograms of samples collected at the side of a road with heavy traffic, where the mix ratio of diesel engine heavy-duty truck was 30–40%, showed little carbon evolution at 920 °C (Fig. 1b).

Several challenges are expected when applying this method in a real workplace: the response factor of MWCNTs must be determined, the interference from background ambient particles must be taken into account, and a standard material for quantitative measurement must be selected. As the profile of the thermogram is expected to be dependent on the crystallinity, size, and metal content of the MWCNTs as well as the degree of agglomeration/aggregation,

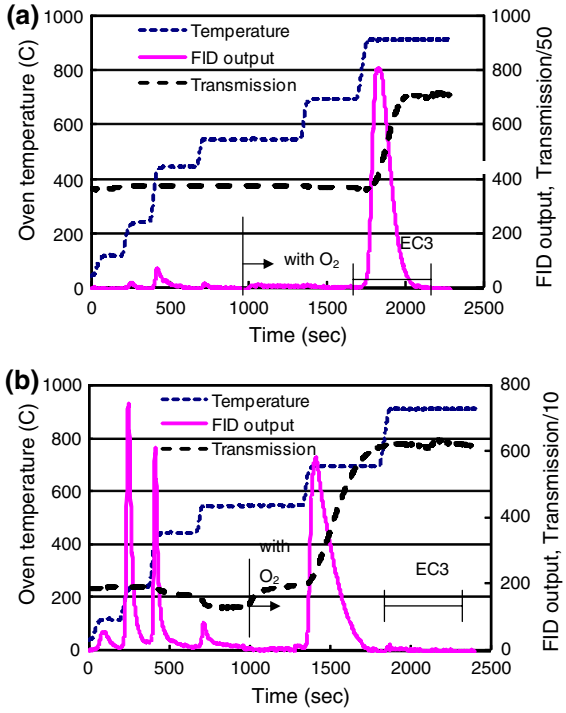

Fig. 1 Thermograms of (**a**) MWCNT and (**b**) Ambient particulate matter collected near heavy-traffic road

care should be taken when this method is used in a CNT facility. Purified CNT products do not evolve easily under these conditions, but real particles suspended in factory air evolve relatively easily. Transition metals, such as iron, present in ambient air or impurities in samples likely work as a catalyst for combustion. During the production process, there will be a mixture of different CNTs from different stages of production, and as a result, a suitable calibration method for quantitative analysis must be developed.

SWCNT handling processes in four factories were monitored by CPC and OPC (Maynard and Baron 2004). The peak calculated mass concentrations during the handling process were 0.15–1.5 mg/m^3 depending on the factory. Both Fe and Ni were used as catalysts in production. Therefore, these were used as a CNT index. Iron impurities were also used to monitor SWCNT concentration in an aerosol generation experiment (Baron et al. 2008) not in the workplace. Such indirect metrics are potentially useful for estimating concentrations of NM particles as long as the contents of the impurities are stable.

Some carbonaceous NMs are used in composites of plastics or metals. Little is known about NP generation during the processing of NP-containing composites. In an analysis at a carbon nanofiber (CNF) handling facility (Methner et al. 2007), bundles of CNFs were observed in samples collected during dry CNF handling by TEM observation. The mass of PM_{10} particles and total carbon concentration in air were elevated during wet saw cutting of the CNF composite. Surface total carbon was higher during the same process.

Fullerenes

A facility for the production of fullerenes, another class of carbonaceous NM, was assessed by using SMPS and SEM analysis (Fujitani et al. 2008). The presence of agglomerates/aggregates were observed by SEM and real-time measurements, but quantitative approaches were not applied. The number concentration of fullerenes outside the factory was higher than that inside the factory.

A field survey was conducted by JNIOSH at a site at which fullerenes (C_{60}) were processed to synthesize lithium-doped fullerenes from purified C_{60} and lithium (JNIOSH 2008). Results of real-time monitoring showed that most particles emitted during this process

were submicron in size. Most of the particles were expected to be agglomerates/aggregates of fullerene, fullerene oxides, and lithium-doped fullerenes, since the starting material in this process is C_{60}, the energy supplied during production is small and the air supplied to the production area was purified, there were no processes that emitted other NPs including soot. In order to confirm this result, SEM observations and chemical analyses were conducted for the particles collected with a Sioutas Cascade Impactor (Misra et al. 2002) during the entire process. Sioutas Cascade Impactor collects particles in four stages from A to D and back-up. The 50% cut-off points are 2.5, 1.0, 0.5, and 0.25 μm if the density of particles is 1.0.

Figure 2 is a SEM image of particles collected with a polycarbonate membrane filter. Elemental analysis showed these particles are composed of carbon, but lithium is not detected by SEM/EDX. Figures 2-AL and 2-AH are SEM images of particles collected on Stage A at low and high magnifications, respectively. Figure 2-CL and 2-CH are that of particles collected on Stage C with low and high magnification, respectively. In Stage A, agglomerates/aggregates of larger sizes are observed than in Stage C. The geometric diameters of the sampled particles greatly differed from their aerodynamic diameters. The morphology observed in high magnification photographs also suggests that the densities of the particles in each stage are different. This kind of disagreement has been reported for SWCNT (Baron et al. 2008). Smaller particles were also observed in Stage A. Impaction may break up the aggregated particles into smaller particles. This point should be noted when the results of EM observation and OPC are analyzed.

HPLC analysis of the same sample showed that C_{60} was determined only for the samples in Stages A and B. The concentration of fullerene was 2 μg/m^3. Fullerene concentration is more sensitive than mass measurement and is expected to be a metric of fullerene exposure in the workplace. Fullerene oxides and metal-doped fullerene may affect the HPLC analysis. They can be separated from fullerene by mass spectrometry which is used for quality control in fullerene industry.

In most of the above cases, since the number concentration of outside air is higher than that of the workplace, the number concentration does not seem to be an appropriate dose metric if it is used by itself. Usually EM is used to distinguish engineered NPs from background NPs with the exception of counting fibers of MWCNT (Han et al. 2008). Since it is quantitative and selective, chemical analysis is one of the best methods of exposure assessment.

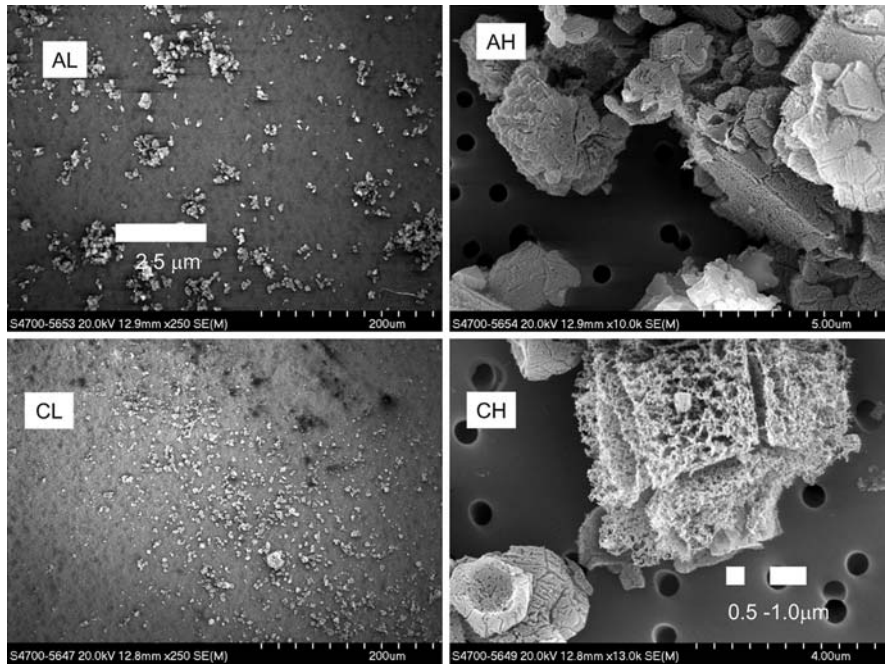

Fig. 2 SEM images of fullerene particles collected by SCI. (AL, AH) Stage A: expected collected size: >2.5 μm; magnification ×250, ×10,000, respectively (CL, CH); Stage C expected collected size: 0.5–1.0 μm; magnification ×250, ×13,000, respectively

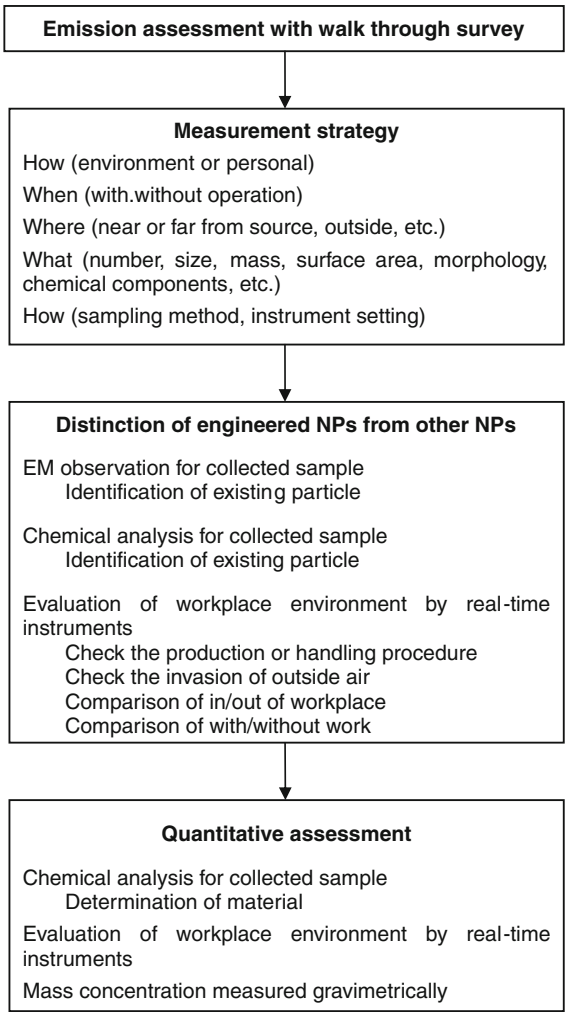

Fig. 3 A probable approach to quantitative measurement of nano-materials in workplace

Approaches to quantitative exposure assessment

From the above examples, probable approaches of quantitative exposure assessment are summarized in Fig. 3. Metrics closely relating to the adverse health effects have not yet been determined; therefore, these approaches are to evaluate the workplace environment and effectiveness of engineering controls. These methods may be helpful in determining strategies for risk management for the production and handling of NMs.

Measurement strategy must be well thought out before conducting an analysis. At present, exposure assessments are performed by analyzing several metrics measured at different locations (inside/outside) and times (with/without work process). The combination of instruments likely determines the quality of the data. Some instruments are not suitable for all facilities due to the emission of solvent vapors from the instruments and the size or weight of the instruments, for example, SMPS and ELPI. The instruments and sampling methods used in the assessment are determined by the nature of the materials and duration of NP generation. The presence of interfering factors from the environment or other work should be investigated before the assessment of NP generation.

Engineered NPs and background NPs can be distinguished by several methods. EM can determine whether the NPs of interest are present by observing morphology and elemental composition. For metal NPs, chemical analysis detects NMs with high sensitivity. The concentration ratios with/without work and inside/outside the facilities provide useful information. Data interpretation should be done after examining the work processes, the other activities at facilities, and the flow of outside air into the facilities.

Quantitative assessments of environmental concentration are conducted both by using real-time measurements and mass measurements including chemical analysis. If the background concentration is stable or low, number concentration is a useful metric: Subtraction of background concentration is a simple way to determine the environmental concentration. In facilities where ambient air is introduced from the outside without any treatment, the amount of bulk material detected by chemical speciation is the best metric.

Future needs

Although surface area is one of the probable dose metrics, there is insufficient information on surface area data regarding the stability and sensitivity of field surveys, with the exception of laboratory studies (Ku and Maynard 2005; Health and Safety Executive 2006; Maynard and Aitken 2007). More information on measurements and their relationship with other metrics is needed. The development of portable and real-time instruments for simultaneous speciation and counting is expected, although these instruments are still under development. Size distribution measurements are necessary for determining whether

nanoparticles are actually present and not agglomerates/aggregates. Sometimes, the size distribution indicates the emission source. The available instruments for measuring size distribution are heavy and bulky, and SMPS have time resolutions of several minutes. A portable instrument for size distribution that has good reproducibility and can detect instantaneous emission is needed for measuring work-related exposure to NPs.

Further research on the toxicology of NMs is necessary to determine appropriate dose metrics for risk management. Analytical methods to measure the dose metric will be investigated in parallel with the dose–response relationship. In the near future, better management systems for NMs will be proposed based on stronger data; these systems will protect workers from hazards and promote workers' health.

Acknowledgments The authors wish to thank Dr Y. Shinohara and the researchers participating in the JNIOSH project "Occupational Health Issue of Nanotechnology Industry," for their support and useful comments.

References

Baron PA, Deye GJ, Chen BT et al (2008) Aerosolization of single-walled carbon nanotubes for an inhalation study. Inhal Toxicol 20:751–760

Birch ME, Cary RA (1996) Elemental carbon-based method for monitoring occupational exposures to particulate diesel exhaust. Aerosol Sci Technol 25:221–241

British Standard Institute (2008a) Nanotechnologies – Part 1: Good practice guide for specifying manufactured nanomaterials. PD 6699-1:2007

British Standard Institute (2008b) Nanotechnologies – Part 2: Guide to safe handling and disposal of manufactured nanomaterials PD 6699-2:2007

Brouwer D, Gijsbers J, Lurvink MWM (2004) Personal exposure to UFP in the workplace: exploring sampling techniques and strategies. Ann Occp Hyg 48:436–453

Bundesanstalt für Albeitsshutz und Albeitsmedizin (Federal Institute for Occupational Safety and Health) (2008) Exposure to nanomaterials in Germany: Results of the corporate survey of the Federal Institute for Occupational Health and Safety (BAuA) and the Association of the Chemical Industry (VCI) using questionnaires

Chow JC, Watson JG, Pritchett LC et al (1993) The DRI thermal/optical reflectance carbon analysis system. Atmos Environ 27A:1185–1201

Dasch J, D'Arcy J (2008) Physical and chemical characterization of airborne particles from welding operations in automotive plants. J Occup Environ Hyg 5:444–454

Demou E, Peter P, Hellweg S (2008) Exposure to manufactured nanostructured particles in an industrial pilot plant. Ann Occup Hyg 52:695–706. doi:10.1093/annhyg/men058

Donaldson K, Li XY, MacNee W (1998) Ultrafine (nanometre) particle mediated lung injury. J Aerosol Sci 29:553–560

Evans DE, Heitbrink WA, Slavin TJ et al (2008) Ultrafine and respirable particles in an automotive grey iron foundry. Ann Occup Hyg 52:9–21

Fujitani Y, Kobayashi T, Arashidani K et al (2008) Measurement of the physical properties of aerosols in a fullerene factory for inhalation exposure assessment. J Occup Environ Hyg 5:380–389

Grassian VH, O'shaughnessy PT, Adamcakova-Dodd A et al (2007) Inhalation exposure study of titanium dioxide nano-particles with a primary particle size of 2 to 5 nm. Environ Health Perspect 115:397–402

Han JH, Lee EJ, Lee JH et al (2008) Monitoring multiwalled carbon nanotube exposure in carbon nanotube research facility. Inhal Toxicol 20:741–749

Hansen ADA, Rosen H, Novakov T (1984) The aethalometer—an instrument for the real-time measurement of optical absorption by aerosol particles. Sci Total Environ 36:191–196

Health and Safety Executive (2006) The assessment of different metrics of the concentration of nano (ultrafine) particles in existing and new industries. Research Report 513

Heitbrink WA, Evans DE, Peters TM et al (2007) Characterization and mapping of very fine particles in an engine machining and assembly facility. J Occup Environ Hyg 4:341–351

Heitbrink WA, Evans DE, Ku BK et al (2009) Relationships among particle number, surface area, and respirable mass concentrations in automotive engine manufacturing. J Occup Environ Hyg 6:19–31

Heymann D, Chibante LPF, Smally RE (1995) Determination of C_{60} and C_{70} fullerenes in geologic materials by high-performance liquid chromatography. J Chromatogr A 689:157–163

Institut de recherché Robert-Sauvé en santé et en sécurité du travial (2009) Best practice guide to synthetic nanoparticle risk management. Report R599

International Standard Organization (2008) ISO/TR 12885:2008 nanotechnologies-health and safety, particles in occupational settings relevant to nanotechnologies

Japan National Institute of Occupational Safety and Health, Field Report Summery 1. Present status of workplace air in a fullerene processing clean-room, and evaluation of performances of particle measurement devices and HPLC analysis. http://www.jniosh.go.jp/joho/nano/files/jniosh/report_fullerene_081028.pdf

Ku BK, Maynard AD (2005) Comparing aerosol surface-area measurements of monodisperse ultrafine silver agglomerates by mobility analysis, transmission electron microscopy and diffusion charging. J Aerosol Sci 36:1108–1124

Kuhlbusch TA, Fissan H (2006) Particle characteristics in the reactor and pelletizing areas of carbon black production. J Occup Environ Hyg 3:558–567

Kuhlbusch TA, Neumann S, Fissan H (2004) Number size distribution, mass concentration, and particle composition

of PM1, PM2.5, and PM10 in bag filling areas of carbon black production. J Occup Environ Hyg 1:660–671

Lam CW, James J J, McCluskey R et al (2004) Pulmonary toxicity of single-wall CNT in Mice 7 and 90 days after intratracheal instillation. Toxicol Sci 77:126–134

Maynard AD, Aitken RJ (2007) Assessing exposure to airborne nanomaterials: current abilities and future requirements. Nanotoxicology 1:26–41

Maynard AD, Baron P (2004) Exposure to CNT Material: aerosol release during the handling of unrefined single-walled CNT material. J Toxicol Environ Health 67:87–107

McCawley MA, Kent MS, Berakis MT (2001) Ultrafine beryllium number concentration as a possible metric for chronic beryllium disease risk. Appl Occup Environ Hyg 16:631–638

Methner MM, Birch ME, Evans DE et al (2007) Identification and characterization of potential sources of worker exposure to carbon nanofibers during polymer composite laboratory operations. J Occup Environ Hyg 4:D125–D130

Misra C, Singh M, Shen S, Sioutas C et al (2002) Development and evaluation of a personal cascade impactor sampler (PCIS). J Aerosol Sci 33:1027–1047

Myojo T, Oyabu T, Nishi K et al (2008) Aerosol generation and measurement of multi-wall carbon nanotubes. J Nanoparticle Res 11:91–99

National Institute for Occupational Safety and Health (2008) Approaches to safe nanotechnology: an information exchange with NIOSH. http://www.cdc.gov/niosh/topics/nanotech/safenano/

National Institute for Occupational Safety and Health (NIOSH) (1994) In: Schlecht PC, O'Connor PF (eds) Method 5040. NIOSH manual of analytical methods (NMAM), 4th ed. U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control and Prevention, Cincinnati, Ohio—DHHS (NIOSH) Pub. 94-113

Oberdörster G (2001) Pulmonary effects of inhaled ultrafine particles. Int Arch Occup Environ Health 74:1–8

Obersdörster G (1996) Significance of particle parameters in the evaluation of exposure-dose-response relationships of inhales particles. Inhal Toxicol 8(supl):73–89

Paik SY, Zalk DM, Swuste P (2008) Application of a pilot control banding tool for risk level assessment and control of nano-particle exposures. Ann Occup Hyg 52:419–428. doi:10.1093/annhyg/men041

Peters TM, Heitbrink WA, Evans DE et al (2006) The mapping of fine and ultrafine particle concentrations in an engine machining and assembly facility. Ann Occup Hyg 50:249–257

Peters TM, Elzey S, Johnson R et al (2009) Airborne monitoring to distinguish engineered nanomaterials from incidental particles for environmental health and safety. J Occup Environ Hyg 6:73–81

Petzpd A, Niessner R (1996) Coulometrische Messung der Russbelastung in der Aussenluft-Verfahrensentwicklung und Anwendung an Messstellen unterschiedlicher Belastung. Gefahrstoffe- Reinhaltung der Luft 56

Poland CA, Duffin R, Kinloch I et al (2008) Carbon nanotubes introduced into the abdominal cavity of mice show asbestos-like pathogenicity in a pilot study. Nat Nanotechnol 3:423–428

Schulte P, Geraci C, Zumwalde R et al (2008) Occupational risk management of engineered nano-particles. J Occup Environ Hyg 5:239–249

Shin WG, Pui DYH, Fissan H et al (2007) Calibration and numerical simulation of nanoparticle surface area monitor (TSI Mpdel 3550 NSAM). J Nanoparticle Res 9:61–69

Shvedova AA, Kisin ER, Mercer R et al (2005) Unusual inflammatory and fibrogenic pulmonary responses to single-walled carbon nanotubes in mice. Am J Physiol Lung Cell Mol Physiol 289:L698–L708

Shvedova AA, Fabisiak JP, Kisin ER et al (2008a) Sequential exposure to carbon nanotubes and bacteria enhances pulmonary inflammation and infectivity. Am J Respir Cell Mol Biol 38:579–590

Shvedova AA, Kisin ER, Murray AR et al (2008b) Inhalation vs. aspiration of single-walled carbon nanotubes in C57BL/6 mice: inflammation, fibrosis, oxidative stress, and mutagenesis. Am J Physiol Lung Cell Mol Physiol 295:L552–L565

Takagi A, Hirose A, Nishimura T et al (2008) Induction of mesothelioma in p53± mouse by intraperitoneal application of multi-wall carbon nanotube. J Toxicol Sci 33:105–116

Thomassen Y, Koch W, Dunkhorst W et al (2006) Ultrafine particles at workplaces of a primary aluminium smelter. J Environ Monit 8:127–133

Warheit DB, Laurence BR, Reed KL et al (2004) Comparative pulmonary toxicity assessment of single-wall carbon nanotubes in rats. Toxicol Sci 77:117–125

Xia XR, Monteiro-Riviere NA, Riviere JE (2006) Trace analysis of fullerenes in biological samples by simplified liquid–liquid extraction and high-performance liquid chromatography. J Chromatogr A 1129:216–222

Zimmer AT (2002) The influence of metallurgy on the formation of welding aerosols. J Environ Monit 4:628–632

Zimmer AT, Biswas P (2001) Characterization of the aerosols resulting from arc welding processes. J Aerosol Sci 32:993–1008