Exposure to Manufactured Nanostructured Particles in an Industrial Pilot Plant

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Objectives: Nanomaterial production and the number of people directly in contact with these materials are increasing. Yet, little is known on the association between exposure and corresponding risks, such as pulmonary inflammation and oxidative stress.

Methods: Condensation Particle Counters, a DustTrak™ and Scanning Mobility Particle Sizer™ quantified real-time size, mass and number concentrations in a nanostructure particle pilot-scale production facility, using a high-temperature gas-phase process, over a 25-day period. Temporal and spatial analysis of particle concentrations and sizes was performed during production, maintenance and handling. Number-based particle retention of breathing mask filters used under real-time production and exposure conditions in the workplace was quantified.

Results: The results demonstrate elevated number concentrations during production, which can be an order of magnitude higher than background levels. Average concentrations during production were $59\,100$ cm^{-3} and 0.188 mg m^{-3} for submicron particles. Mask filters decreased particle number concentrations by >96%.

Conclusions: This study demonstrates real-time worker exposure during gas-phase nanoparticle manufacturing. Qualitative and quantitative analysis of emission sources and concentration levels in a production plant is accomplished. These results are important for workers, employers and regulators in the nanotechnology field as they provide information on encountered exposures and possibilities for mitigation measures.

Keywords: CPC; exposure; nanoparticles; particulate matter

INTRODUCTION

Nanotechnology has gained greater interest in recent years as a result of the increase in engineered nano- and nanostructured particle production and their use in a growing number of sectors and products. The production of particles in smaller size ranges changes and often enhances a material's characteristics.

Inhalation is the main exposure pathway for particulate matter (PM) and the most critical for nanoparticle uptake (Hoet *et al.*, 2004; Brüske-Hohlfeld *et al.*, 2005; Oberdörster *et al.*, 2005a). A review by Oberdörster *et al.*, (2005b) examines potential human health effects resulting from exposure to nanoparticles and nanomaterials. Studies have demonstrated increased toxic effects per mass dose of ultrafine metal particles compared to their larger counterparts (Zhang *et al.*, 2000; Zhang *et al.*,

2003) and a better correlation of the effects to surface area rather than mass (Maynard and Kuempel, 2005; Oberdörster *et al.*, 2005a). Equally important are the uptake and translocation capabilities of nanoparticles to target organs in the body, such as the spleen and liver (Kreyling *et al.*, 2002; Hoet *et al.*, 2004; Brüske-Hohlfeld *et al.*, 2005), and the brain (Oberdorster *et al.*, 2004). In fact, an inverse relation of size to uptake has been described for certain particles (Kreyling *et al.*, 2002). The toxicological properties of nanomaterials are not fully identified. Material's characteristics may change with decreasing size, making it difficult to derive toxicological properties from bulk chemical characteristics. Previous studies have proposed building on ultrafine particle epidemiological and pathological experience. The lack of information on risks emanating from exposure to nanomaterials has led to concerns that the nanotechnology sector is not fully prepared to deal with these (Gewin, 2006).

Current research suggests that size alone may be one determinant of toxicity. Ultrafine titanium

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dioxide and carbon black displayed a greater effect on macrophage phagocytosis than the equal mass of fine particles (Renwick *et al.*, 2001). These observations indicate that nanotoxicity may be related to the increased surface-to-volume ratio of smaller particles. No limit for a cutoff size was identified (Donaldson, 2004). Nevertheless, some experts suggest that there is no reason to give extra weight to studying the effect of 'free' nanoparticles versus that of larger structures with bound nanoparticles (Morgan, 2005).

A published study on carbon nanotubes investigated potential human exposure levels to engineered nanoparticles combined with a toxicological analysis (Maynard *et al.*, 2004; Shvedova *et al.*, 2005). Experience on occupational monitoring during nanoparticle production is still in its infancy, with concerns voiced in establishing an appropriate metric and empirical method (The Royal Society, 2004). Occupational thresholds for exposures are mass based, apart from the case of asbestos fibers (NIOSH, 2005). Scientific reviews examining concerns of nanoparticle exposure and nanotoxicology and evaluating possible threshold metrics for particles in the nanometer range found that bulk mass concentration is insufficient and suggest particle number and possibly surface area as better indicators (Aitken *et al.*, 2004; Brouwer *et al.*, 2004; Oberdörster *et al.*, 2005a). However, the available evidence does not permit a generalization (Maynard and Kuempel, 2005). Schulte *et al.* (2008) stress the importance of identifying the tasks and processes leading to increased exposures to nanoparticles in the workplace, as well as the assessment of the airborne nanoparticle concentrations of relevant metrics to provide the basis for engineering and administrative controls (Schulte *et al.*, 2008). This calls for the simultaneous investigation of a number of physical–chemical properties for a holistic exposure assessment. This would involve the determination of metrics such as mass, number, surface area, along with an analysis of the chemical composition. The airborne particulates may have altered chemical compositions from the end product due to physical processes, surface reactions and contamination, leading to changes in their toxicological properties. Therefore, while toxicological studies are completed on pure nanoparticles, the toxicological profile of the inhaled nanomaterials should also be assessed.

Available commercial nanoparticle production methods are divided into four categories, being mechanical (grinding), wet production, vapor deposition synthesis and gas-phase processes (Aitken *et al.*, 2004). Gas-phase productions occur via uniform nucleation of a supersaturated vapor phase followed by particle growth via coagulation and condensation (Aitken *et al.*, 2004). The authors suggest this production method as the most important for inhalation exposure to nanoparticles (Aitken *et al.*, 2004). Reviews have concluded that no significant research investigating potential control measures with respect to exposure to nanoparticles has hitherto been accomplished (Aitken *et al.*, 2004; Maynard and Kuempel, 2005). The adequacy and effectiveness of protective measures largely depend on particle behavior, such as their sizes, shape and tendency to form agglomerates. Limited data indicate that conventional controls such as ventilation, filters and containments may be sufficient (Maynard and Kuempel, 2005).

Mask efficiencies to various airborne inert particles have been investigated in laboratories as well as under workplace conditions (Nelson *et al.*, 2000; Bidwell and Janssen, 2004; Lee *et al.*, 2005; Kim *et al.*, 2007; Eninger *et al.*, 2008). However, the number of studies regarding natural and engineered nanoparticles is limited. Additionally, performance studies focusing on number concentrations are scarce (Balazy *et al.*, 2006; Kim *et al.*, 2007; Eninger *et al.*, 2008).

This study was completed at a nanostructured particle production facility, which at the time was a developmental pilot plant. The facility employed a gas-phase production technique to produce nanostructured particles. The end product consists of metal-based nanoparticles embedded in a larger porous oxide matrix. Hence, this study examines workers' real-time exposure to airborne nanostructured particle concentrations produced in an occupational setting. Hereafter, the term nanostructures refers to the total of airborne particles produced during the manufacturing stage, from 0.004 to 1 μm, based on the instrumental detection capabilities in terms of size range.

The goals of this study were (i) to identify and quantify the sources of nanostructured particle emissions in a production facility; (ii) to characterize the emitted particles in terms of airborne concentration and size and (iii) to identify, quantify and propose measures for the mitigation of the potential exposure relative to task.

## MATERIALS AND METHODS

Instrumentation

A Scanning Mobility Particle Sizer (SMPS model 3936, TSI Inc.) was employed for the size distribution measurements. The instrument consisted of a Condensation Particle Counter (CPC model 3775, TSI Inc.) and an Electrostatic Classifier (EC model 3080, TSI Inc.), holding a Differential Mobility Analyzer (DMA model 3081) and a bipolar charger (model 3077, TSI Inc.) (TSI 1998; TSI, 2005; TSI, 2006). Two further CPCs were used (CPC 3022A and 3007, TSI Inc.), which differed in lower cutoff sizes (7 and 10 nm, respectively) from CPC 3775 (4 nm). An aerosol monitor, DustTrak™ (model 8520, TSI Inc.), was applied to determine particle

mass concentration. An impactor with a cutoff of 1.0 μm (PM1.0) was used to allow sampling from 0.1 to 1.0 μm (100–1000 nm). This is similar to the range of the CPC 3007 (10–1000 nm), especially when taking into account that mass measurement tends to be dominated by larger sizes. This means that for mass the readings of the two instruments can be compared. For thermal anemometric measurements, VelociCalc Plus (model 8386A, TSI Inc.) and two Air Velocity Transducers (model 8450, TSI Inc.) were employed. The latter measure air velocity, while the former quantifies air velocity, temperature, relative humidity and differential pressure. The transducers were applied for determining air velocities in a set location, while the VelociCalc Plus was normally located near the particle counters.

A filter-testing chamber (Fig. 1) was designed to determine mask-filter particle retention in the workplace during real-time operating conditions and exposure situations. Sampling during this experimental run was done in position P1 (see Fig. 2). Particle-laden air during regular production was drawn in with a vacuum pump (model EMA 63-11 F115-2, Euromotori, Macherio, Italy) and controlled by a rotameter (model KSK-1080A K20 00, Kobold Messring GmbH, Hafheim, Germany). Tubing (320 and 130 mm) was used before and after the rotameter for the connection. Pressure drop between the two compartments was measured with a high-precision manometer (model 612a, Schiltknecht Messtechnik AG, Switzerland).

Instrumental settings during the measurement procedures are recorded in Table S1 (see supplementary material, available at *Annals of Occupational Hygiene* online). All instruments, apart from the SMPS system and the CPC 3022A, were calibrated by the manufacturer. Deviations between CPC models 3007 and 3022A, resulting from differences in the counting modes, saturating liquids, cutoff diameters and accuracies of the instruments, were quantified. The comparison of all 1 min means resulted in a linear regression with a correlation of $r^2 = 0.97$. The data set included measurements under background and production conditions and therefore reflected two diverse environments with respect to concentration levels. As an accuracy of ±20% is indicated for both instruments, the deviation between the two CPCs was considered acceptable. No adjustment
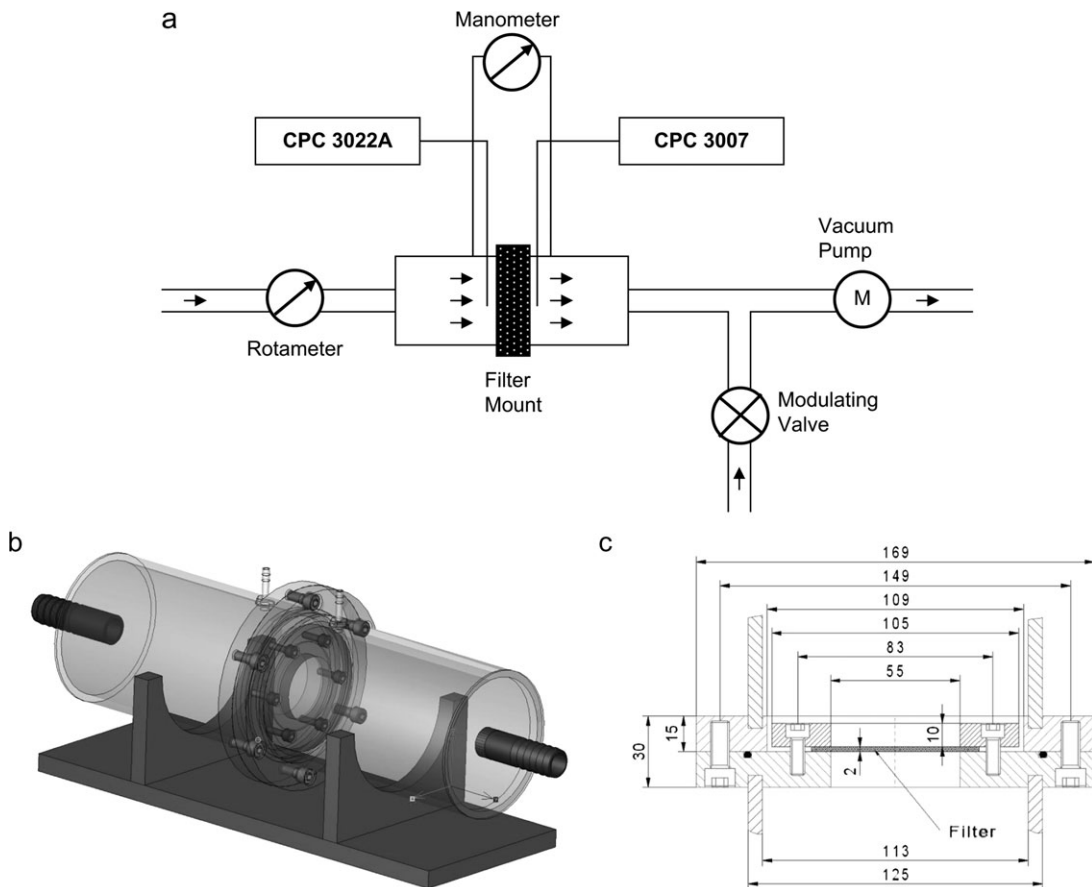
Fig. 1. (a) Schematic diagram of mask filter-testing apparatus. (b) Filter-testing chamber. (c) Cross-sectional diagram with chamber dimensions (millimeter).

was applied to the data. Calibration of the CPC 3775 system by the manufacturer required a correction factor of $100/(100 - 41.5)$ to the readings due to low inlet flow (Zerrath, A, TSI Inc.).

Experimental plan

Seven sampling locations were chosen to capture the spatial and temporal variation in particle levels (Fig. 2). The sampling inlets were positioned ~1.2 m above the floor level to quantify the breathing concentration between the standing and sitting working position. In total, 113 h of measurements were completed over a 25-day period. Events such as machine operation and changes, employee activities or atypical incidents were recorded on logging sheets to support the analysis of the monitoring results. Workers' activities included reactor maintenance and cleaning, mechanical adjustments to the reactor system and its operation, powder handling and packaging and workplace cleaning.

As the sampled particles were not chemically differentiated, those of a similar size range derived from other sources, such as traffic or other industrial processes within the production hall, were investigated by quantifying background mass and number concentrations. Generally, background levels were determined each day prior to production start. These measurements were complemented by additional background data collected at varying positions within the site to capture diurnal variations. In gen-

eral, activity levels from the surrounding sites were low.

In order to establish reasons for the significant interday variability in mass background concentrations, data from the Swiss National Air Pollution Monitoring Network were acquired for ambient outdoor PM_{10} concentrations. Outdoor concentrations could be relevant, as infiltration factors from 0.35 to 0.93 have been observed for the case of $PM_{2.5}$ in various settings (Mitchell *et al.*, 2007).

Temporal measurements were performed with all instruments in the same position and for each location. This allowed quantifying concentrations for specific working areas over time and comparing the instrumental readings. Under the spatial mode, the instruments were separated into two positions at a time, allowing insight into particle distribution dynamics and the identification of secondary particle sources. A reference position (P5) was selected near the reactor system and combined with the mid- (P1) and the far-field position (P3), as well as with a location near a mechanically agitated powder handling and packaging station (P6), in the office (P4) and outside the production area (P2) (Fig. 2).

High short-term exposures during maintenance procedures have been identified in nanoparticle production (Aitken *et al.*, 2004). Therefore, regular reactor cleaning and the exhausts of the vacuum cleaner (model NT72/2 Eco Tc, Alfred Kärcher GmbH & Co. KG) were monitored.
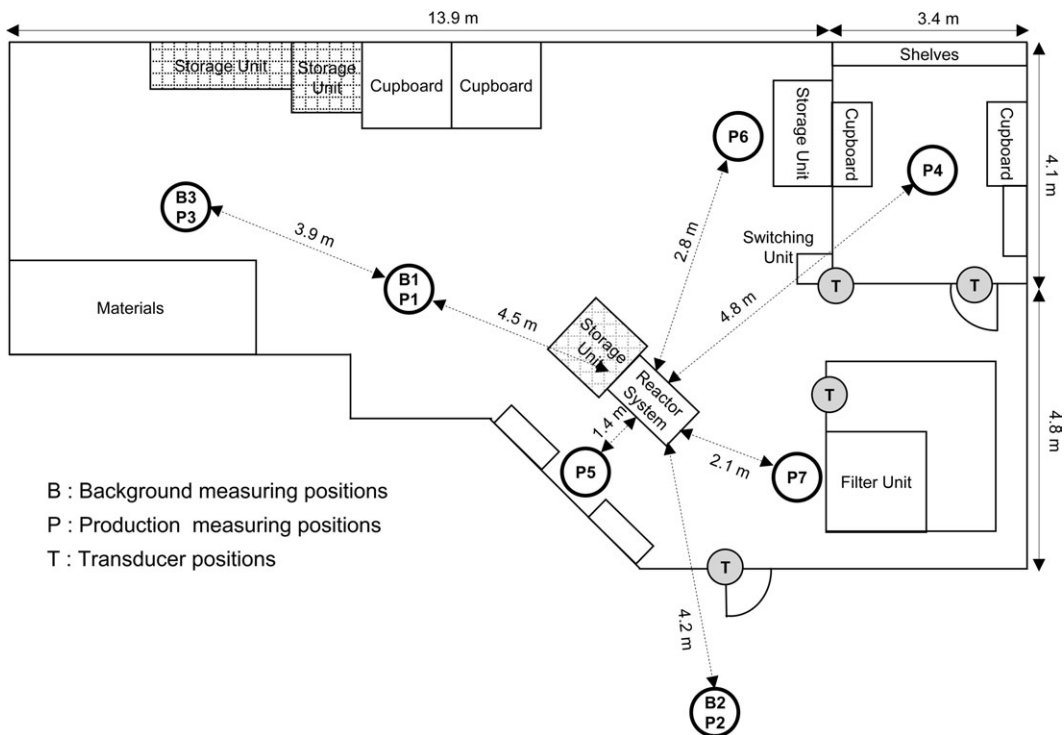

Fig. 2. Measurement positions at the industrial production pilot plant.

Table 1. Filter-testing results

Filter type (standard)	Flow rate		Pressure drop, Δp		Protection factor[a], P	Retention, R[b]
	Start ($m^3\ h^{-1}$)	End ($m^3\ h^{-1}$)	Start (Mbar)	End (Mbar)	Mean (-)	Mean (%)
3M 2135 (FFP3)[c]	2.15 ± 0.05	2.00 ± 0.05	5.55 ± 0.05	5.35 ± 0.05	$(9.39 \pm 2.66) \times 10^2$	99.890 ± 0.031
	1.05 ± 0.05	1.00 ± 0.05	3.15 ± 0.05	3.20 ± 0.05	$(9.74 \pm 2.76) \times 10^3$	99.989 ± 0.003
3M 5935 (FFP3)[c]	1.55 ± 0.05	1.50 ± 0.05	5.45 ± 0.05	5.65 ± 0.05	$(1.50 \pm 0.42) \times 10^4$	99.992 ± 0.002
	1.00 ± 0.05	1.00 ± 0.05	3.35 ± 0.05	3.40 ± 0.05	$(3.76 \pm 1.06) \times 10^4$	99.997 ± 0.001
3M 9320 (FFP2)[d]	3.00 ± 0.05	2.45 ± 0.05	3.65 ± 0.05	3.95 ± 0.05	$(3.03 \pm 0.86) \times 10^1$	96.661 ± 0.944
	2.15 ± 0.05	1.90 ± 0.05	3.35 ± 0.05	3.45 ± 0.05	$(1.24 \pm 0.35) \times 10^2$	99.187 ± 0.230
Dräger type 680 (FFP3)[c]	1.00 ± 0.05	1.00 ± 0.05	5.45 ± 0.05	5.45 ± 0.05	$(2.37 \pm 0.67) \times 10^5$	99.999 ± 0.000

[a]Protection factor is the fraction of the number concentration (cm^{-3}) before the filter over that after the filter.
[b]Retention is defined as the proportion of incoming particles retained by the filter (see supplementary material, available at *Annals of Occupational Hygiene* online).
[c]FFP3 according to EN 143:2000 (DIN, 2000).
[d]FFP2 according to EN 149:2001 (DIN, 2001).

The retention capability in terms of particle number concentration of four different types of mask filters was evaluated, two of which were used at the investigated production site and the remaining two were used at other nanoparticle production sites (H. Schulz, personal communication) (Table 1 and Table S2). In line with the requirements of standard EN 143:2000, an averaging period of 30 s was applied (DIN, 2000), after flushing the system for 3 min to remove the residual particles trapped in the chambers. Then each filter was tested for 37 min under a high and low continuous flow rate. The latter was adjusted near 1.00 $m^3\ h^{-1}$, which is slightly above a light activity level inhalation rate for adult men, while the high flow rate was set to 2.15 $m^3\ h^{-1}$ to approximate the inhalation rate under moderate activity for adults (Paustenbach, 2002). During the measurements, the flow rates were recorded at the beginning and every 10 min thereafter. Additionally, mass concentration and environmental conditions were monitored in proximity to the testing setup.

RESULTS

*Number and mass concentrations*

Inter- and intraday variability and spatial variation were examined for all background measurements. The mean of 20 daily average background levels was 0.052 ($\pm 1\%$) mg m^{-3} and 8512 ($\pm 20\%$) cm^{-3}. Three sample days were excluded from the data set due to special conditions. These days were excluded because the outdoor gate was constantly open, which did not correspond to the normal working practice and substantially influenced indoor concentrations. The inter- and intraday relative standard deviation (RSD) of the daily background mass concentration averages was 203 and 7.37%, respectively. Number concentrations showed inter- and intraday variabil-

ities of 30.8 and 14.6%, respectively. Slightly lower number concentrations were generally recorded in the beginning of the day, most likely due to differences in background activity. Variability increased toward the start of production as a result of preparatory procedures immediately before production start.

Comparison of indoor versus outdoor mass concentrations during the monitoring period showed that if two outliers in the data were excluded, a correlation of $r^2 = 0.6$ between the daily PM_1 background values derived within the hall and the mean PM_{10} during daytime was found. The two extreme values might be caused by an outdoor source nearby or from within the hall, rather than by general urban environmental levels.

Figure 3 depicts the variation in the number and mass concentration profiles for all positions combined from 17 measurement days. The minimum and maximum, after excluding the outliers, are represented by the whiskers of the box plots. Daily mean average steady-state concentrations over these measurement days were 59 100 ($\pm 20\%$) cm^{-3} and 0.188 ($\pm 1\%$) mg m^{-3} with an RSD of 29.7 and 184%, respectively. Highest number counts reached 136 000 ($\pm 20\%$) cm^{-3} on Day 17. The maximum mass concentration recorded was 1.340 ($\pm 1\%$) mg m^{-3} on Day 8. Measurement days excluded from the final pilot-plant production data set included days without any production or operation of the production unit, fragmentary days and measurements outside the production area.

Figure 3 demonstrates considerable variation in the data of up to one order of magnitude difference during the reactor cleaning, starting and steady-state phases. The decreasing trend in the steady state and the increase in variability toward the end of the steady-state phase reflect the variability in production rate and duration of operation of the reactor system. Since the latter varied between days, the average
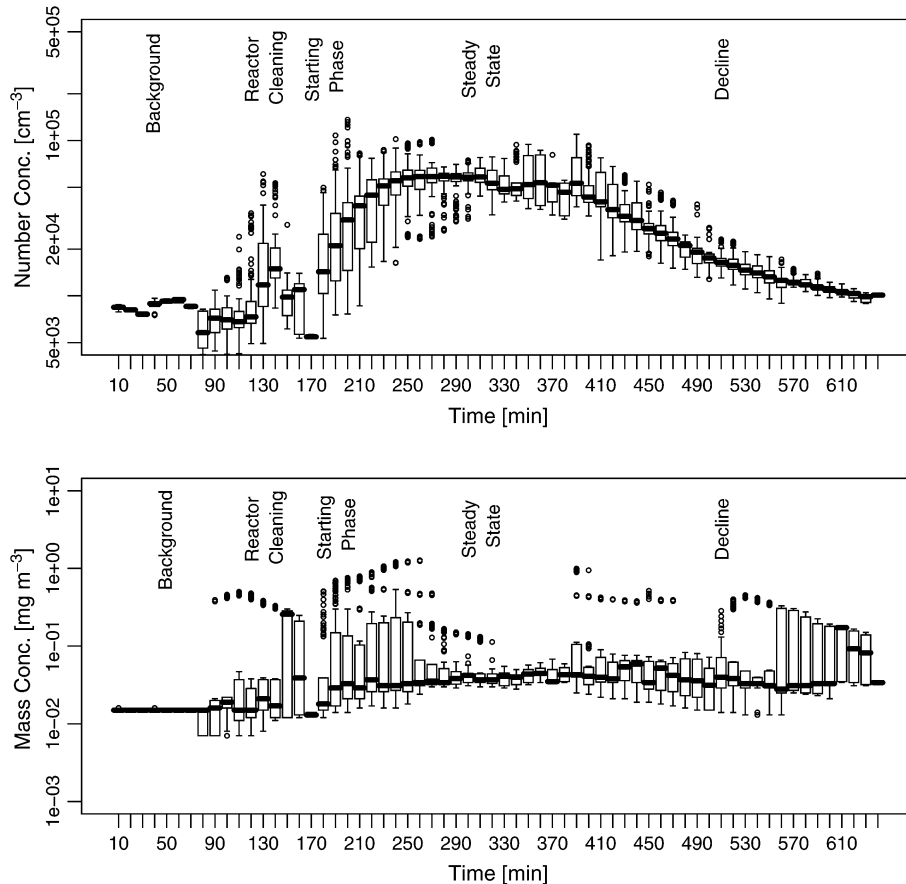
Fig. 3. Average number and mass variation of all measurement days and positions. The production phases are (i) background phase (0–125 min), (ii) reactor system cleaning phase (125–174 min), (iii) starting phase (174–234 min), (iv) steady-state phase (234–381 min) and (v) decline phase (381–441 min). The box plots indicate the median and 25th and 75th percentile. The whiskers indicate the minimum and maximum levels after the outliers, values >1.5 times the inter-quartile range, have been excluded. The open circles represent outliers.

values toward the end of the steady-state phase were calculated from a decreasing number of measurements. Other reasons for variability include configuration changes and variability in the daily production plan, such as in the pattern of production and secondary activities.

The average number concentration profile reflected the production profile rather well. For instance, the cleaning of the reactor system was coupled to a short increase in number concentration. The start of production led to a steady rise for ∼1 h before reaching a steady-state resembling stage. Incremental reductions in production rate during the production course were followed by a decrease in particle levels. The end of production is depicted with an exponential decline of the concentration until background levels were reached, lasting ∼3 h. In contrast to the number concentration profile, no correlation of average mass concentrations with the production course was observed. A correlation between the two concentration metrics was observed only on some days (compare Fig. 4c,d versus Fig. 4a,b,

for example). This unstable correlation between mass and number concentration and mass and production profile is the reason that particle emission sources are only described in terms of number concentrations hereafter.

Emission sources

The major emission source in this pilot-plant production facility was the production unit. Particle production rate was reflected both in the profile and magnitude of the airborne concentration, as early incremental decreases in production rate caused a drop in concentration. Particle resuspension was not relevant. This was established by operating all system units as during regular operation, except for the reactor system. During this trial, no substantial increase in particle levels was recorded (see Figure S1, supplementary material, available at *Annals of Occupational Hygiene* online).

Agglomeration as a loss process was considered to be not significant for the submicron particles due to their size and concentration (Preining, 1998), and

the main removal process was therefore the air exchange rate ($0.706 \ h^{-1}$).

A one-box model, based on particle number conservation, was employed to estimate submicron particle emission rate from the average number concentration profile (equation 1). In this model, the volume of the workplace is modeled as one homogeneously mixed box. Workplace concentrations are calculated as a function of emission, ventilation rate and time elapsed from emission start (Keil, 2000). The air exchange rate and particle emission rate were assumed to be constant. The only particle removal process considered was via the air exchange of the workplace, which was estimated by fitting an exponential curve to the particle number concentration profiles in the declining phases after production stopped. Background levels were subtracted and emissions from production only were estimated.

$$V\frac{dC(t)}{dt} = E - Q \times C(t), \qquad (1)$$

where $C(t)$ is the concentration in the workplace (cm^{-3}); V is the workplace volume (cm^3); Q the ventilation rate ($cm^3 \cdot min^{-1}$) and E the particle emission rate (min^{-1}).

The solution to the differential equation for the particle concentration at steady state, C_∞, results to equation 2. From this, the average emission rate of submicron particles was estimated to be $3.18 \cdot 10^{11}$ min^{-1}.

$$C_\infty = \frac{E}{Q}. \qquad (2)$$

The investigated production site was a developmental pilot plant and adjustments and changes were continuously made, therefore contributing to the variability. Fugitive powder emissions were occasionally observed from separate operations (P6) such as cleaning and non-routine powder handling. Mechanical handling of the powder before packaging showed no significant influence on the concentrations derived in positions P6 and P5 even though particle agitation occurred. Conversely, transferring of product powder resulted in small increases in number concentrations (see supplementary Figure S3, available at *Annals of Occupational Hygiene* online).

Maintenance procedures were also a source of considerable particle emissions. On Day 19, routine cleaning of the reactor system with a vacuum cleaner resulted in increased concentrations, with peaks
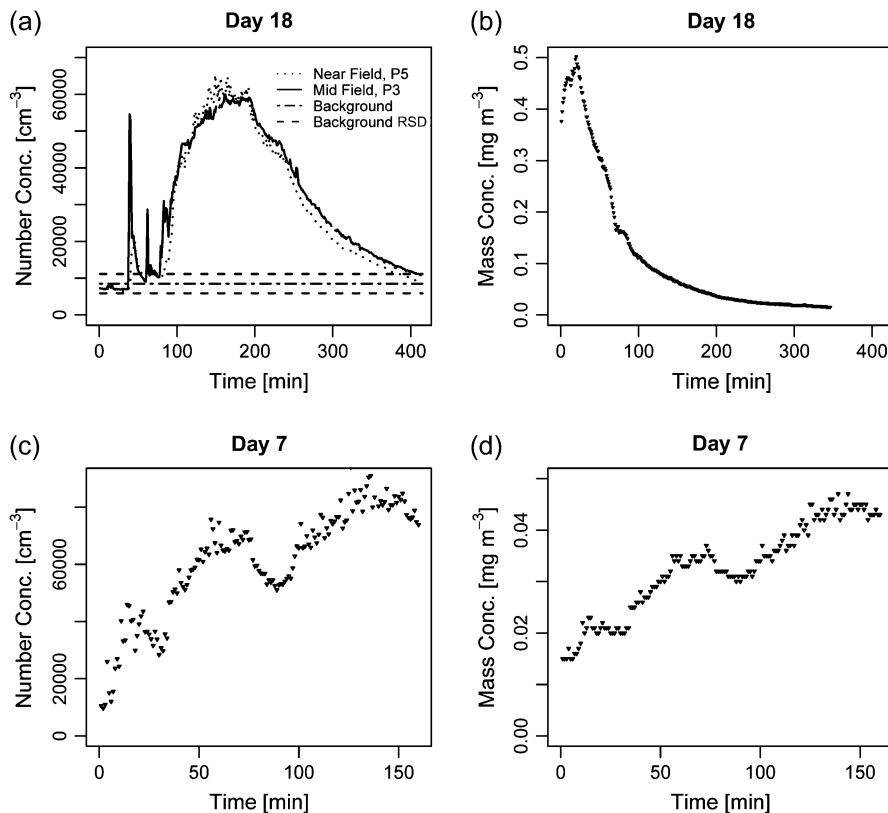
Fig. 4. Mass and number concentration profiles. Graphs (a) and (b) refer to the simultaneous measurements taken in position P3 on Day 18. Graphs (c) and (d) refer to the simultaneous measurements taken in position P7 on Day 7. Graph (a) displays the spatial distribution (positions P3 and P5) of the number concentration during a typical production day (Day 18). The first and second peak of Fig. 4a refer to the reactor system cleaning and preparatory work, while the third peak is the production process.

reaching almost 50 000 cm^{-3} at P6 (see supplementary Figure S3, available at *Annals of Occupational Hygiene* online). During a second day of maintenance with hardly any vacuum cleaning, concentrations remained <20 000 cm^{-3}. The vacuum cleaner was equipped with a filter of the German 'Dust Class M' applicable for dusts with a Maximale Arbeitsplatzkonzentration (MAK) value ≥0.1 mg m^{-3}. This category of filter specifies a transmission of <0.1%. Even though the vacuum cleaner was equipped with one of the highest standard filters, it was a second relevant emission source for short-term exposure. However, as no chemical speciation was done, the nature of these particles was unknown.

Spatial variation and ambient conditions

The comparison of the spatial variation in concentrations was focused on the steady-state number concentrations. Only a small difference was observed between simultaneously derived measurements in different positions within the production site (e.g. Fig. 4a), which could be a result of fast thermal mixing. On the smaller timescale, distinct differences were detected, such as during reactor system cleaning (Fig. 4a). A considerable difference was recorded between the near-field position (P5) and outside the production site (P2) (see supplementary Figure S2, available at *Annals of Occupational Hygiene* online).

The effect of the ambient environmental parameters was investigated. The air velocity, temperature and relative humidity displayed no influence on the number and mass concentrations during background or production phases (see supplementary material, available at *Annals of Occupational Hygiene* online).

Size distribution

During the SMPS 3936 measurements, temperature and relative humidity ranged from 25.5 (±0.3)°C to 34.4 (±0.3)°C and from 35 (±3) to 58 (±3)%, respectively. Despite being within the ambient operating conditions, the SMPS system indicated elevated condenser temperatures. This condition affected particles <20 nm, which may not have been sufficiently activated and therefore counted unreliably.

The size distribution results are based on measurements of one production day (Day 25). Although limited, it allowed deriving an impression of the average size distribution at the production site. Measurements were conducted in the range of 20–630 nm, which included the peak concentration (Fig. 5). However, the absolute concentrations were underestimated due to the higher diffusion losses at the low flow conditions.

Figure 5 displays the average size distribution for the starting, steady state, early and advanced decline. Identical channel resolutions of 64 channels per decade of particle size were applied and therefore the number concentrations are directly comparable. Although variability in total number concentration during the starting and decline phase was high, the shape of the distribution remained stable in all phases. The maximum concentration for the starting phase was ~160 nm, while for the steady state and early decline it was ~200 nm. The size distribution of the advanced decline illustrates considerably lower concentrations for all sizes, but proportionally more larger particles compared to the previous distributions.

Personal protective equipment

The aim of the evaluation of mask filters was not to confirm compliance with filter standards but to investigate particle retention under field conditions with respect to number concentration. In this study, temperature and relative humidity during the filter testing were relatively constant: 19.6 (±0.3)°C to 23.2 (±0.3)°C and 30 (±3) to 38 (±3)%, respectively. As these conditions are fairly constant and within the range specified by the norms (i.e. 24 ± 8°C and ≤60%), the effect of temperature and relative humidity on filter performance was not investigated.

The filter protection factor, *P*, characterizing the fraction of incoming to outgoing particles, was estimated for each filter using number concentrations. Furthermore, filter resistance, quantified in terms of the pressure drop, Δp, across the filter, was quantified (Table 1).

Mean particle number retentions were between 96.661 (±0.944) and 99.999 (±0.000)% during the measurement period (Table 1). Resistance ranged between 3.15 (±0.05) and 5.65 (±0.05) Mbar, while pressure drop tended to increase with time. A difference of a factor of 7.6 in the protection factor between the analyzed filter classes (3M 9320 and 3M 2135) was detected under the same flow rate. Along with the enhanced protective performance, resistance of the higher standard filtering face piece (FFP) filter was also higher. Additionally, filter performance under low flow rates yields a higher retention (Table 1). Performance of filter type 3M 2135 decreased by a factor of 10 for a 2-fold higher flow rate.

Increasing impact area of the same standard revealed large differences in the protection factor. A difference of more than an order of magnitude was observed when comparing the flat 3M 2135 filter to the grooved Dräger filter type 680 under similar flow rates. However, the Dräger filter was the only preused sample and therefore clogging may possibly account for part of the observed increased performance (Brown, 1993).

DISCUSSION

A qualitative process review of a nanostructured particle production facility and a quantitative evaluation of real-time workers' exposures in relevant
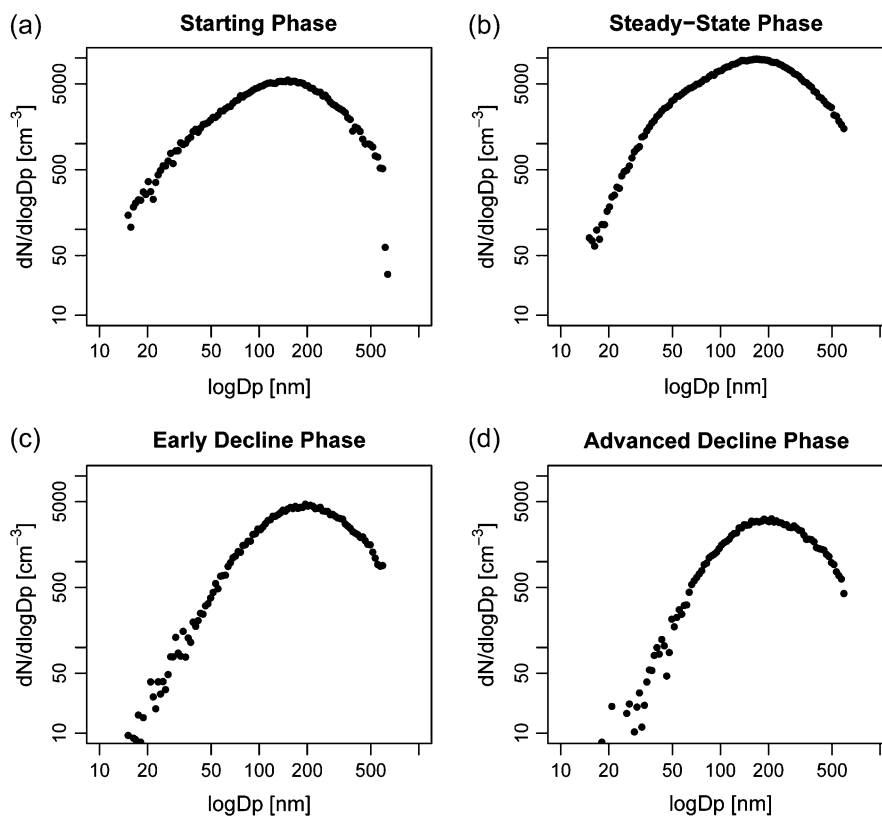
Fig. 5. Average size distributions of particles by phase (a–d). Measurements were taken on Day 25. Identical channel resolutions were applied.

metrics for exposure assessment in nanotechnology are presented. Gas-phase processes have been described as the only type of nanoparticle production methods, which can lead to inhalation exposure of primary nanoparticles as a result of direct reactor leaks (Aitken *et al.*, 2004). This study confirms elevated exposure in a gas-phase nanostructured particle production setting. The production unit was the main particle source in the investigated facility, thereby explaining the good correlation between number concentration and production stages. The vacuum cleaner was a second important source for short-term exposure, increasing number but not mass concentrations, suggesting the use of cleaners with higher standard filtration systems (Maynard *et al.*, 2004). In contrast, particle handling and processing during product postproduction mechanical agitation did not yield a substantial rise in submicron particles. Similarly, a previous study found no substantial increase in concentrations during events of powder handling (Maynard *et al.*, 2004).

In contrast to number concentration, the average background mass concentration demonstrated large day-to-day variability. Only days with low background mass and comparatively high production number concentrations displayed a correlation with production. Maximum number and mass concentrations were recorded on different days. Comparably, no direct correlation between mass and number concentration time series was found for carbon nanotube exposures (Maynard *et al.*, 2004). In the investigated case, the average size distribution indicates that a large proportion of the measured particles were in the low size range. While measures based on particle numbers are size independent, mass concentrations are dominated by larger particles, thereby explaining the lack of correlation.

Concentrations inside the production area were approximately twice the simultaneously measured concentrations in the corridor, but no significant spatial differentiation was found within the investigated site. This uniform distribution could be explained by thermal mixing in the production area. The production unit was also relatively large, displayed multiple fugitive emissions and hence could probably not be referred to as a point source. The size distribution measurements showed a stable distribution throughout all phases with a small shift in the peak.

The encountered concentrations appear moderate when contrasted to other literature values. Concentrations measured in workplaces, households and urban environments can be similar or much higher

than the steady-state concentrations obtained at this site (Zhu *et al.*, 2002; Stephenson *et al.*, 2003; Maynard *et al.*, 2004). However, as the concentrations are derived under different conditions, the outlined comparison can only provide an indication for the corresponding order of magnitude. Furthermore, differences in exposure times and particle-specific toxicities cannot be disregarded. Submicron particles generated as by-products of human activity and engineered nanostructures may have similar general adverse effects, but may vary considerably with respect to the specificity and severity of the health effects.

Airborne particle size distribution measurements during production revealed a concentration peak ~200 nm and approximately one-third of the measured particles at the production site had a mobility diameter <100 nm. Depending on the particular properties of the produced nanostructures, characteristic nanotoxicological effects may therefore also be relevant for the investigated case.

More than 70% of the nanostructured particles are in the accumulation mode as defined by Preining (1998). These particles are expected to remain relatively long in ambient air and therefore would have time to disperse throughout the production site supporting the observed homogeneity in concentration and also be transported to the outdoor environment via air exchange.

The average size distributions of the phases reveal a small shift to larger particle sizes. This shift, especially after production ceased, may be an influence of the background particle size distribution. The average background level was 24% of the production steady state and 59% of the advanced decline level derived that day. The size distribution of background particles may therefore have had an influence on the overall size distribution, in particular during the starting and the decline phase, when the contribution from production was smaller. Further measurements are necessary to establish the relevance or not of agglomeration and background particles on the size distribution at the investigated production site.

Filter retention is not only relevant for personal protection but also for ventilation and cleaning systems. The findings of this study are in line with suggestions that due to Brownian motion, high filter performance is expected for particles in the nanometer range (Aitken *et al.*, 2004; Mark, 2004; Maynard and Kuempel, 2005). The retentions measured under production conditions at the investigated production plant were between 96.66 and 99.99% in terms of number concentration. Similarly, investigated commercial filter performances of nanoparticles in the size range of 3–20 nm displayed 99.99% efficiencies for number concentrations (Kim *et al.*, 2007). As filter retention depends on particle size, direct comparison with the applicable mass-based standards cannot

be performed. However, the measured average size distribution indicates a mean particle diameter close to the most penetrable particle size (MPPS). Comparing filter performance with those in terms of MPPS shows that both the 94 and 99% retention is met for the FFP2 and FFP3 filters, respectively (DIN, 2000; DIN, 2001).

Filter testing in this study was performed under moderate flow rates. While filter resistance increased during the measurements, the corresponding flow rates decreased over the testing period by up to 18%. The demonstrated rise in resistance can be due to clogging, as demonstrated in other studies (Novick *et al.*, 1992; Brown, 1993). Even though the breathing pattern was not simulated, the results indicate that a 2-fold increase in flow rate, which could correspond to a breathing rate under intense workload, reduces filter retention by a factor of 10. As expected, higher retention for larger impact areas under the same flow rate and standard was demonstrated. The importance of flow rates on the protection efficiency has been described in studies examining this issue (Stevens and Moyer, 1989; Gardner *et al.*, 2005). The present results are in agreement with observations that lower flow rates are not only desirable in terms of breathing resistance but also favorable for filter efficiency.

The evaluation of respiratory protection equipment in this study was confined to the assessment of filter performance. However, in terms of overall respirator performance, face-seal leakage predominantly around the nose, cheek and chin is generally more relevant than filter efficiency (Aitken *et al.*, 2004; Mark, 2004; Lee *et al.*, 2005) and should be investigated for submicron particles in more detail.

CONCLUSIONS

Potential hazards and risks with respect to health effects from exposure to nanoparticles are still unknown. In this study, the issue of workers' exposure in an industrial production pilot plant was investigated and essential factors for quality control and good operating conditions, such as emissions, concentrations and safety measures, were evaluated and quantified. In this production setting, employing a gas-phase production system, emissions of submicron and nanoparticles occur. Furthermore, the concentration patterns can be directly correlated to the process phases. This may be important for other occupational environments employing gas-phase techniques for nanoparticle production. Continued research in other settings will provide the knowledge to qualitatively and quantitatively assess whether airborne nanoparticle exposure in general is an issue in these production workplaces. This work and results on exposure in a nanostructured particle production facility are relevant for health officials,

companies and those working in nanoparticle production, as it allows for minimization of risks in the absence of toxicological data and provides indications for a safe occupational environment.

SUPPLEMENTARY DATA

Supplementary data, Tables S1 and S2 and Figures S1–S3 can be found at http://annhyg.oxfordjournals.org/

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