Assessment of Personal Exposure to Airborne Nanomaterials

A Guidance Document

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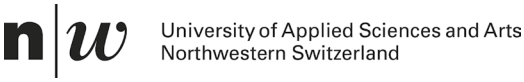

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Content

Introduction

The use of manufactured nanomaterials (MNMs)[1] has increased at a constant pace over the recent years. Their applications range from scratch resistant or self-cleaning surface coatings, via enforced polymers to enhanced cosmetics. Besides the tremendous new opportunities offered by these novel materials, concerns have been raised because of potential adverse health effects that may arise if MNMs are taken up by the human body [1]. While human exposure to MNMs may in principle occur during any stage of the material's lifecycle, it is most likely in workplaces, where these materials are produced or handled in large quantities or over long periods of time. Inhalation is considered as the most critical uptake route, because the small particles are able to penetrate deep into the lung and deposit in the gas exchange region. Inhalation exposure to airborne nanomaterials therefore needs to be assessed in view of worker protection.

Exposure to airborne particles can generally best be assessed by measuring the individual exposure in the personal breathing zone (PBZ) of an individual. The PBZ is defined as a 30 cm hemisphere around mouth and nose [2]. Measurements in the PBZ require instruments that are small and lightweight. The individual exposure specifically to MNMs has not been assessable in the past due to the lack of suitable personal samplers and/or monitors. Instead, most studies related to exposure to MNMs have been carried out using either bulky static measurement equipment or not nanospecific personal samplers. In recent years, novel samplers and monitors have been introduced that allow for an assessment of the more nanospecific personal exposure to airborne MNMs. In the terminology used in nanoIndEx, samplers are devices that collect particles on a substrate, e.g. a filter of flat surface, for subsequent analysis, whereas monitors are real-time instruments that deliver information on the airborne concentrations with high time resolution. Scientifically sound investigations on the accuracy, comparability and field applicability of these novel samplers and monitors had been lacking. This lack of knowledge was the nucleus for starting the project "Assessment of

[1] In the literature, manufactured nanomaterials are also termed engineered nanomaterials (ENMs) or nanoobjects and their agglomerates and aggregates (NOAA). Although their exact definition may be slightly different, these terms are used synonymously in this document.

Individual Exposure to manufactured nanomaterials by means of personal monitors and samplers" (nanoIndEx).

Partners involved in the nanoIndEx project are:

- Federal Institute of Occupational Safety and Health (BAuA, Berlin, Germany),
- French Alternative Energies and Atomic Energy Commission (CEA, Grenoble, France),
- University of Applied Sciences and Arts Northwestern Switzerland (FHNW, Windisch, Switzerland),
- Institute of Occupational Medicine (IOM, Edinburgh, UK),
- Institute of Energy and Environmental Technology e. V. (IUTA, Duisburg, Germany),
- Institute for Hazardous Substance Research (IGF, Bochum, Germany),
- Catholic University of the Sacred Heart (UCSC, Rome, Italy).

The three-year project started on June 1st, 2013, and has been funded under the frame of SIINN, the ERA-NET for a Safe Implementation of Innovative Nanoscience and Nanotechnology. The aim of the project was to scrutinise the instrumentation available for personal exposure assessment concerning their field readiness and usability in order to use this information to generate reliable data on personal exposure in real workplaces and to eventually widely distribute the findings among the interested public. This Guidance Document you are holding in your hands summarises the key findings of the project.

Initially, the literature was thoroughly studied to identify suitable personal monitors and samplers. Those instruments that were identified as suitable and that have been available for the project underwent intensive laboratory investigations concerning their accuracy and comparability. The investigations covered a broad range of aerosol and particle properties, including the full range of morphologies from spherical over agglomerated to fibrous particles. Such studies are of utmost importance in terms of quality assurance and to eventually judge whether potential differences in concentrations measured in the PBZ and in the background or far field are significant. An overview of the available personal samplers and monitors and their accuracy, comparability and field applicability is presented in chapter 2. Standard Operation Procedures (SOPs) have been prepared for the operation of all personal samplers and monitors and are freely available on the project's website www.nanoindex.eu.

Exposure measurements in the field require a clear strategy. The exact strategy can vary depending on the local settings in the workplace and may need to be tailored to the questions to be tackled. The choice of instruments is affected by the measurement strategy. If, for example, task based exposure with short-lived spikes in the concentrations are to be assessed, the use of personal monitors with high time resolution is inevitable. To the contrary, for the determination of shift-based averages, samplers may also be used. If personal exposure to a certain chemical species shall be assessed, then with the currently available technology, this can only be achieved by particle sampling and subsequent chemical analysis of the deposit. Placement of the instruments for monitoring of the background or far field concentrations is also an important component of the measurement strategy. Chapter 3 of this Guidance Document presents suggestions on how to conduct field measurements of personal exposure.

After completion of a measurement campaign, the collected data have to be analysed and stored. Besides the measurement data, contextual information on the surveyed workers, their activities, the workplaces etc. have to be gathered. Especially in case of monitors with high time resolution of e.g. one second, one may easily lose overview of the huge data set. nanoIndEx has developed data collection and analysis protocols, based on the Nano Exposure and Contextual Information Database (NECID), that simplifies the data management and analysis. Chapter 4 provides recommendations concerning data collection, analysis and storage.

Field studies have been conducted within nanoIndEx, to bring the knowledge on the instrumentation, the measurement strategy and the data collection and analysis into practice. The investigated workplaces varied from laboratories, where nanoparticles are being produced or characterised, via a pilot plant for the production of engineered nanomaterials in an intermediate scale to large scale industrial production. The aim of the field studies was not only to collect data on personal exposure, but also to learn more about the field readiness of the samplers and monitors. The field studies are summarised in chapter 5.

„The outcome
of any serious research
can only be to make
two questions grow
where only one question
grew before“

THORSTEIN VEBLEN
(1857–1929)

(Not only) In the sense of Thorstein Veblen's quote, nanoIndEx was a serious research project, because we experienced numerous surprises and novelties during the course of the project. In one case, one of the instrument types reacted completely differently than expected, because of an interference with the sampling tube material. In another case, the placement of the instruments used for background monitoring in field measurements turned out to be more critical than anticipated. Chapter 6 shares the expected and unexpected lessons we have learned during the project with you to make room for new questions rather than making you grow the exact same questions again.

This Guidance Document is intended to present you the state of the art in personal exposure assessment for nanomaterials. While the focus of the project was on exposure to manufactured nanomaterials in workplaces, most findings are also directly applicable to the assessment of exposure to non-engineered nanoscale particles, e.g. in the environment. We hope that you will find this brochure interesting and useful. For further information, please also refer to our webpage www.nanoindex.eu.

Chapter 2

Measurement and sampling techniques including accuracy, comparability and field applicability

2.1. Metrics issues

Current occupational exposure limits for MNMs are set as mass concentration limits. For nanofibres, fibre concentration limits may be imposed in analogy to asbestos. At present, no occupational exposure limits based on lung deposited surface area (LDSA) or particle number levels are under discussion. However, in this regard it is important to note that even if number concentration is often dominated by nanoscale particles, such as MNMs, their mass is usually negligible compared to that of coarse particles. Consequently, other metrics than mass should be taken into account in order to make an adequate and comprehensive evaluation of exposures to MNMs in workplaces. Unfortunately, it is not yet clear which key particulate parameters (mass, surface area, number or size distribution) could be the most relevant measurement unit with regard to MNM-related occupational health issues.

Of the currently available commercial personal instruments, few aim at deriving mass concentrations. These include X-ray fluorescence-based mass determination of filter samples, which, however, can only be applied to nanoparticles of specific elemental composition signature before a particle background free of this signature element. Likewise, the mass of graphitic carbon-based MNMs may be quantified before the ubiquitous carbon-containing background by EC/OC analysis of filter samples. Knowledge of the background profile and composition is mandatory for the application of such techniques. The black carbon exposure may be assessed by radiation absorption of filtered dust and aerosols. The particle background must thus always be studied before or after a work task assessment and, if possible, even in parallel by monitoring the supply air.

Personal monitoring instruments using electrical nanoparticle detection principles generally apply unipolar diffusion charging to determine LDSA concentrations and in some cases also the number concentration. The number concentration can also be determined by condensation particle counters (CPCs). However, as of now only a single personal CPC exists.

2.2. Personal monitors

Within nanoIndEx, three types of personal monitors were thoroughly characterised: (1) the Miniature Diffusion Size Classifier DiSCmini (Testo, Titisee-Neustadt, Germany, identical with miniDiSC) [3], (2) the Aerasense nanoTracer (oxility, Eindhoven, the Netherlands) [4] and (3) the partector (naneos, Windisch, Switzerland) [5]. All three instruments are based on diffusion charging of the nanoparticles, followed by the detection of currents on the femto-Amp level. All instruments can measure the LDSA concentration, the DiSCmini and the nanoTracer can additionally also measure particle number concentration and average particle diameter. In all three instruments, aerosols enter the instrument and are charged in a unipolar diffusion charger, where they acquire a charge which is nearly proportional to the particle diameter ($q \sim dx$, with x approximately 1.1), and, by coincidence, also nearly proportional to the LDSA. The ion trap removes excess ions remaining after the charging process. The proportionality to LDSA is not exact, but it can be thought of as a good approximation to LDSA at least in the size range of 20–350 nm. Figure 1 shows the relation of charge to LDSA over the range of 5–10,000 nm:

The graph shows clearly that the charge acquired is a reasonable approximation (± 25 %) for the LDSA in the size range of 20–350 nm. If ± 30 % deviation is tolerable, the size range can be extended to 400 nm. Larger deviations occur outside of this size range: for micronsized particles, the LDSA inferred from charging is about ten times too low, for very small particles around 10 nm, the LDSA inferred is about twice as high as in reality. It should be noted that the contribution of sub-20 nm particles to the total LDSA concentration is typically low, whereas the deviation for large particles can be quite

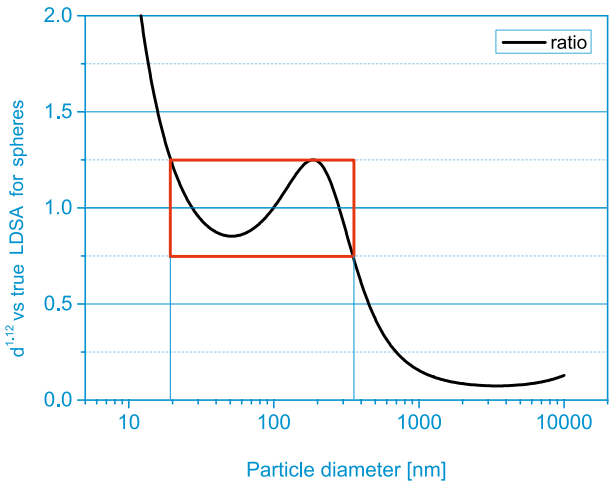


FIGURE 1: Charge acquired by the particles vs calculated LDSA for spherical particles.

significant. Further uncertainties to the LDSA determination apply, such as differences due to particle material and morphology, and different breathing patters of individuals. As can be seen from Figure 1, there is also an uncertainty regarding the calibration of the instruments; instruments could be calibrated at say 50 or 100 nm – no standard on calibrating LDSA has been established as yet, and therefore instruments of different manufacturers may easily disagree systematically by 10–20 %.

In addition to these three monitors, a Personal Ultrafine Particle Counter (PUFP C100, Enmont, Cincinnati, USA) was briefly tested towards the end of the project. The PUFP C100 is a personal water based condensation particle counter that measures the particle

INSTRUMENT ▸	MINIDISC DISCMINI	NANOTRACER		PARTECTOR	PUFP C100	PUFP C200	MICROAETH AE51
							
SIZE (H x W x D) (cm x cm x cm)	18 x 9 x 4.5	16.5 x 9.5 x 3		13.4 x 7.8 x 2.9	19 x 11 x 7	13 x 10 x 7	11.7 x 6.6 x 3.8
WEIGHT (g)	670	750		400	1,000	750	280
PARTICLE SIZE RANGE (nm)	10–300	Fast mode 20–120	Advanced mode 10–300	10–10,000	≥ 4.5		–
CONCENTRATION RANGE	10^3–10^6 #/cm^3	0–10^6 #/cm^3		0–2*10^4 µm^2/cm^3	0–2*10^5 #/cm^3		0–1 mg BC/m^3
METRIC	NC/d_p/LDSA	NC	NC/ d_p/LDSA	LDSA	NC		Black Carbon concentration
ACCURACY	± 30%	± 1,500 cm^{-3}		± 20%	± 10%		±1 µg BC/m^3
SAMPLE FLOW (lpm)	1	0.3–0.4		0.5	0.3		0.05/0.1/0.15/0.2
TIME RESOLUTION (s)	1	3	16	1	1		1/10/30/60/300
BATTERY LIFE TIME (h)	6–8	7		15	3.3– 6		6–24

TABLE 1: Specifications of personal monitors.

number concentration. The newer version C200 is mainly identical with the C100, but smaller and quieter. Table 1 provides an overview of the specifications of the available personal monitors.

2.2.1. Partector

The partector is the simplest and smallest of the available personal monitors. Its scheme and a photograph are shown in Figure 2.

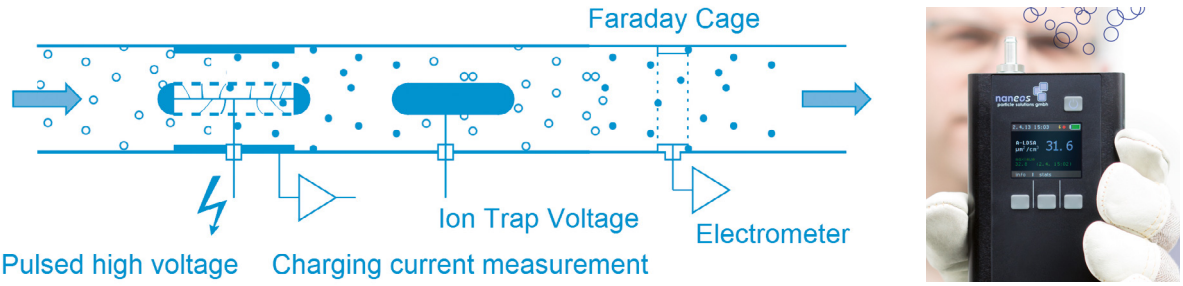


FIGURE 2: Scheme (left) and photograph (right) of the partector. [6]

The unipolar charger is pulsed on-off so that clouds of charged particles are generated periodically. [5] These charge clouds pass through a Faraday cage connected to an electrometer, which "sees" the charge clouds and reacts to them by always keeping the entire cage electrically neutral, i.e. the charge on the Faraday cage is always the opposite of that inside the cage. By measuring the charge flowing to the cage, the charge on the aerosol can be inferred. The signal of the electrometer has a sinusoidal shape, and its amplitude is a measure for the total charge on the particles, and is calibrated for LDSA concentration. This AC-type measurement has the big advantage that electrometer zero offset drifts are automatically compensated for, and thus temperature/humidity variations hardly affect the device, and its start-up time is very short (16 s) compared to the others. The technical specifications of the partector are summarised in Table 1. An enhanced version of the partector is additionally equipped with an electrostatic precipitator that can collect particles onto a TEM grid for subsequent analysis. The instrument, based on the measured concentration, recquires an adequate sampling time.

2.2.2. DiSCmini

The DiSCmini has two electrometer stages that can be used to infer more information about the particles. [3] Particles are charged continuously and detected first in a "diffusion stage" consisting of a stack of stainless steel grids, where preferentially smaller particles are deposited by diffusion. The larger particles have a higher probability of passing through this stage, and end up in a filter stage, where all particles are collected. The schematic of the instrument is shown in Figure 3. By measuring the ratio of the two electrometer stages, the average particle size is inferred, and the particle number concentration is calculated from the total current and the particle size information.

The DiSCmini measures both currents in parallel, and thus determines the LDSA concentration, particle number concentration, and average particle size. DiSCmini is the only instrument that uses a pre-separator (impactor) that removes all incoming particles greater than 700 nm. The particle size range for accurate LDSA concentration measurements is limited to 20–400 nm (see above). For number concentration measurements, there is in principle no lower size limit. Only the charging efficiency decreases with decreasing particle size such that a very high concentration may be needed in order to produce sufficient current. nanoIndEx experiments showed that DiSCmini can still measure the

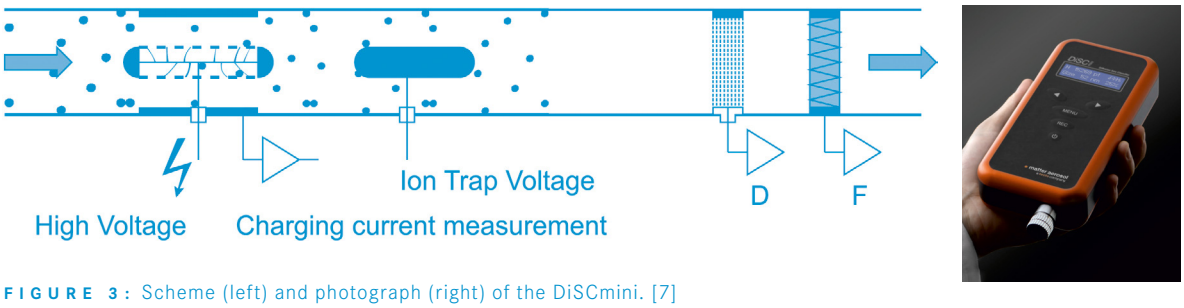


FIGURE 3: Scheme (left) and photograph (right) of the DiSCmini. [7]

number concentration of 10nm particles with reasonable accuracy. Technical specifications are given in Table 1.

2.2.3. nanoTracer

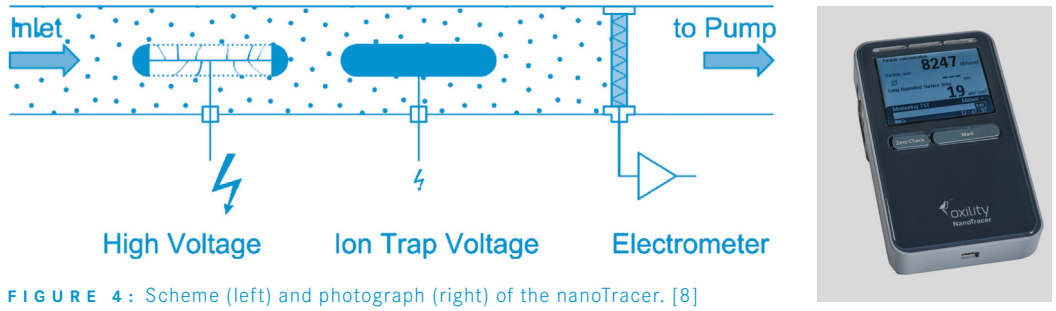


FIGURE 4: Scheme (left) and photograph (right) of the nanoTracer. [8]

The Aerasense nanoTracer uses a switched electrostatic precipitation zone to achieve essentially the same measurement capabilities as the DiSCmini with a single electrometer detection stage. [4] The precipitator preferentially removes small particles from the gas stream, i.e. when it is turned on, the electrometer measures mostly large particles; when the precipitator is off, the electrometer measures all particles. As in the case of DiSCmini, the total current, measured when the precipitator is off, is proportional to the LDSA concentration and the average particle diameter and particle number concentration are determined from the ratio of the two currents. Technical specifications of the nanoTracer can be found in Table 1.

2.2.4. PUFP C100/C200

The Personal Ultrafine Particle Counter (PUFP model C100, Enmont, Cincinnati, USA) [9] is a water based condensation particle counter. The incoming aerosol is exposed to an atmosphere, supersaturated with water vapour. The vapour condenses onto the particle surfaces and makes them grow to optically detectable sizes. The water reservoir lasts for 6 h continuous operation before it needs to be refilled. The C100 is equipped with a GPS receiver that tracks the movements of its user and allows for linking the exposure to the location. However, this feature is intended for outdoor use and usually does not work for (indoor) workplace measurements.

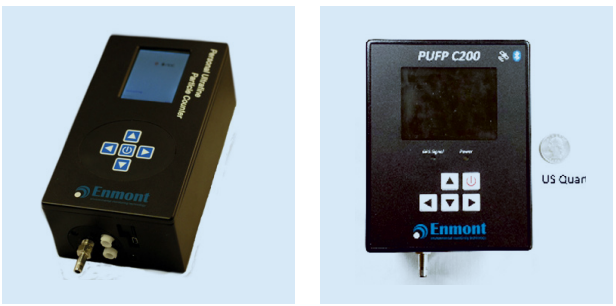


FIGURE 5: Photograph of the Personal Ultrafine Particle Counter; left: PUFP C100, right: PUFP C200. [10]

A newer version of the PUFP, the model C200, which is smaller, lighter and quieter than the C100 but with otherwise identical specifications has just been introduced. Technical specifications of both the C100 and C200 are given in Table 1.

2.2.5. Black carbon monitor MicroAeth AE51

The black carbon monitor (BCM, see Figure 6) device MicroAeth (model AE51, Aethlabs, San Francisco, CA, USA) is a portable, self-contained and battery-powered aerosol monitor that uses airflow filtration and is capable of measuring Black Carbon (BC) with up to one minute time resolution. The instrument uses real-time absorption measurements of a white, PTFE-coated borosilicate glass fibre filter. Infrared absorption at 880 nm is interpreted as a real-time signature for the mass of black carbon particles on the filter. Quantification can be achieved by using the absorption coefficient for black carbon of 16.6 m^2/g from the literature. [11] The obtained result corresponds to an equivalent black carbon concentration. By using an inlet cyclone with $PM_{2.5}$ at 50 ml/min flow rate and $PM_{1.6}$ at 100 ml/min, the device can be used as a nanoparticle monitor.

Any particles with absorption at 880 nm deviating from that of black carbon will cause incorrect mass predictions. It has been reported that the concentration of carbon nanofibres and -tubes can be determined with the MicroAeth device. [12] However, the author reported the response of the BCM to drop with increasing nanotube filter load already at about 1/10 of the manufacturer's recommended filter load. In addition, nanotube-specific calibration was reported to be necessary.

2.2.6. Accuracy and comparability of the personal monitors

In the nanoIndEx project, a large comparison study was performed in the laboratory to characterise the accuracy (compared to reference instruments) and comparability (deviations between N devices of the same type) of the personal monitors DiSCmini, partector and nanoTracer for 17 test aerosols with particle diameters ranging from 10–700nm. The study has been conducted in the nanoTestCenter at IGF.

As reference, a scanning mobility particle sizer (SMPS) was used, which records the entire particle size distribution, from which all parameters measured by the personal monitors can be calculated. In general, a good accuracy [14] and good comparability was found for LDSA for all devices investigated. [15] The average deviation from the reference instrument was about ± 10 % in all cases, and the variability around ± 20 % (with a few outliers). A general dependence on particle morphology or concentration could not be found. Only for particles with diameters below 20 and above 250 nm, larger deviations were found as expected and described in the introduction of this chapter.

For the particle diameters, the average deviation was approximately - 20 % for the DiSCmini, and +5 % for the nanoTracer, the number concentration was overestimated by 30 % on average by the DiSCmini and 10 % by the nanoTracer. The variability between instruments in the number concentration was about twice as high (± 20 %) than in LDSA – this is not surprising, since the LDSA measurement is a direct measurement of a current, whereas the particle diameter and number concentration are inferred by assuming parameters of the particle size distribution which are not necessarily correct. Nevertheless, the performance of the personal monitors is clearly satisfactory, as even expensive stationary nanoparticle detectors are usually specified to an accuracy of ± 10 % at best.

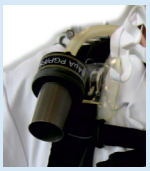
A loan unit of the PUFP C100 has only shortly been available towards the end of the project. It has undergone a smaller study to compare results obtained with the C100 with results from stationary reference CPCs. A water based (TSI model 3787) and a butanol based (TSI model 3776) CPC were

FIGURE 6: MicroAeth AE51 Black carbon monitor. [13]

used as references. Measurements were conducted with hygroscopic NaCl and hydrophobic DEHS particles of different sizes and concentrations. The results show that the C100 typically agreed within ± 10 % with the reference CPCs. However, the instrument was almost blind for pure hydrophobic DEHS particles. When the dispersed DEHS contained only minor impurities, the agreement with the butanol based reference CPC was again much better. The water based reference CPC showed in principle the same behaviour against hydrophobic DEHS particles. For workplace or ambient measurements, it is expected that this finding does not limit the usability of the PUFP C100, since it is very unlikely that such highly pure hydrophobic particles or droplets are encountered.

2.3. Personal samplers

In contrast to direct-reading personal monitors, personal samplers are devices that collect particles for subsequent analysis. Typical substrates used in personal samplers are filters for the analysis of the mass concentrations and/or chemicalcomposition of the particles, and flat surfaces (e.g. Si wafer) or TEM grids for electron microscopic analysis of the particle size and morphology or – if coupled with energy dispersive X-ray fluorescence spectroscopy (EDX or EDS) – the chemical composition.

INSTRUMENT	PGP	NANOBADGE		NRD	TEM PARTECTOR	ESPNANO 100	TPS
							
		2013	2015				
SIZE (H x W x D) (cm x cm x cm)	(1)	16.5 x 9.5 x 3	16.5 x 9.5 x 3	–	14.2 x 7.8 x 2.9	15.24 x 10.16 x 7.62	15 x 6 x 3.5
WEIGHT (g)	(1)	150	255	–	430	907	320
PARTICLE SIZE RANGE (nm)	(1)	10–4,000		< 300	10–10,000	20 nm-supermicron range	20–600
SAMPLE FLOW (lpm)	2	0.6	1	2.5	0.45	0.1	0.001–0.01
SUBSTRATE	gold-coated track-etch membrane filter	polycarbonate track-etched membrane filter quartz filter		nylon mesh screens	TEM grid	TEM grid metallic/silicon substrate	nickel TEM grid
BATTERY LIFE TIME (h)	depends on the pump	> 8		depends on the pump	15	6–24	8

(1) Depends on model (E, A or FAP)

TABLE 2: Technical specifications of commercial personal samplers.

Measurement strategies that use sampling instruments and subject sampled aerosol ensembles to microscopic particle (or fibre) analysis can provide valuable information on this particle spectrum with respect to number, size and morphology. However, missing agglomerate and particle densities together with a determination of only the 2D-projected particle area currently limit the reliability of such indirect particle mass estimation.

The sampling of workplace atmospheres for such an individual particle-based analytical approach requires at least an approximate knowledge of the particle (number) concentration. The reason is that individual aerosol particle analysis does not tolerate too high filter coverage, which would lead to attaching or overlapping particles. In order to keep the filter coverage at an acceptable level, appropriate sampling durations must be chosen based on prevalent particle concentrations. Such an approach is applied, e.g., by the partector TEM device. It integrates the LDSA concentration during TEM grid sampling to stop electrostatic deposition at TEM grid coverage optimised for individual nanoparticle analysis. If not integrated in the instrument, the use of an additional monitor may be required to estimate the optimal sampling time. An overview of the technical specifications of the personal samplers is given in Table 2.

2.3.1. Filter based samplers

2.3.1.1. Personal sampling system PGP

FIGURE 7: The PGP-FAP sampler.

The personal sampling system PGP (German: personengetragenes Probenahmesystem) is a personal filter holder system for collecting particles of different fractions. The PGP-EA is equipped with a well defined porous polyurethane foam as a pre-selector for the E- (respirable) and A- (alveolar) fractions. For occupational workplace sampling of fibres, the PGP version PGP-FAP can be used. It is generally operated at 2 l/min airflow with the filter surface being oriented downwards. The face velocity of the filter is kept at a low level by a wide inlet nozzle of 30 mm diameter, see Figure 7. Technical specifications can be found in Table 2.

2.3.1.2. NANOBADGE

FIGURE 8: The NANOBADGE sampler (2015 version).

The NANOBADGE (NANO INSPECT, Alcen group, Paris, France and French Alternative Energies and Atomic Energy Commission CEA, Grenoble, France) is a lightweight, battery-operated and portable device, which can collect airborne particles directly in the breathing zone of a worker. The sampler is connected to a cassette, whose filter is analysed offline by X-ray fluorescence spectroscopy (XRF) providing a cumulative mass-based quantification of the chemical elements present on the filters. The measurement of the engineered nanoparticle concentration by their constitutive element using XRF represents a very powerful strategy, because it is a way to get rid of the existing high and fluctuating background level of natural and anthropogenic nanoparticles. Moreover, it is a non-destructive analytical technique, meaning that the same sample can be characterised further with other techniques such as scanning electron microscopy (SEM). The instrument is provided with filter units (single use) in individual zip

bags and personal ID badge (personal use, one for each person operating the sampler). The filter unit is a sealed cassette containing a polycarbonate track-etched membrane to collect particles and is equipped with a RFID chip to store data (sampling time, date, flow rate, errors, worker ID, sample ID, ...). Track-etched membranes allow particle collection for subsequent analysis by XRF (elemental composition and concentration) and SEM-EDX (particle size, morphology and chemical identification). It can be equipped with two different pre-separators to remove coarse particles (impactors for respirable fraction, i.e. with d_{50} = 4 µm or $PM_{2.5}$) that were not evaluated in this study.

After sampling, the cassettes are extracted from the NANOBADGE and sent directly for analysis and subsequent data restitution (e.g. elemental mass concentration in the breathing zone averaged over the total sampling time).

Table 2 provides the technical specifications of the NANOBADGE. The 2013 version of the NANOBADGE sampler was evaluated in the project nanoIndEx and is referred herein as 'NANOBADGE'. A single on-off switch makes the NANOBADGE device robust and very simple to use. The sampling time and the sampled volume are automatically logged into the RFID tag located in the sampling unit.

The device is equipped with red/green lights and an alarm sound to warn the user about any malfunction (e.g. inlet clogged, discharged battery, etc.). The encountered errors are logged. The device has been recognised to be comfortable, securely fastenable and does not restrict the mobility of the user. However, in quiet workplaces the device is perceived by some users as noisy and producing annoying vibrations[2].

2.3.1.3. Nanoparticle Respiratory Deposition (NRD) sampler

The personal nanoparticle respiratory deposition (NRD, Zefon International, Ocala, FL, USA) [16] sampler was developed to be used as a full-shift personal sampler that selectively collects nanoparticles in a workplace atmosphere. To do this, firstly a new collection criterion, namely the nanoparticulate matter (NPM), was devised in order to get the target collection efficiency of the sampler. The NPM is the fraction of airborne particles that would deposit in the human respiratory tract by Brownian diffusion. Based on this criterion the NRD sampler would collect all particles smaller than 300 nm, the minimum deposition for sub-micrometre particles, that when inhaled can deposit anywhere in the respiratory tract (see Figure 9).

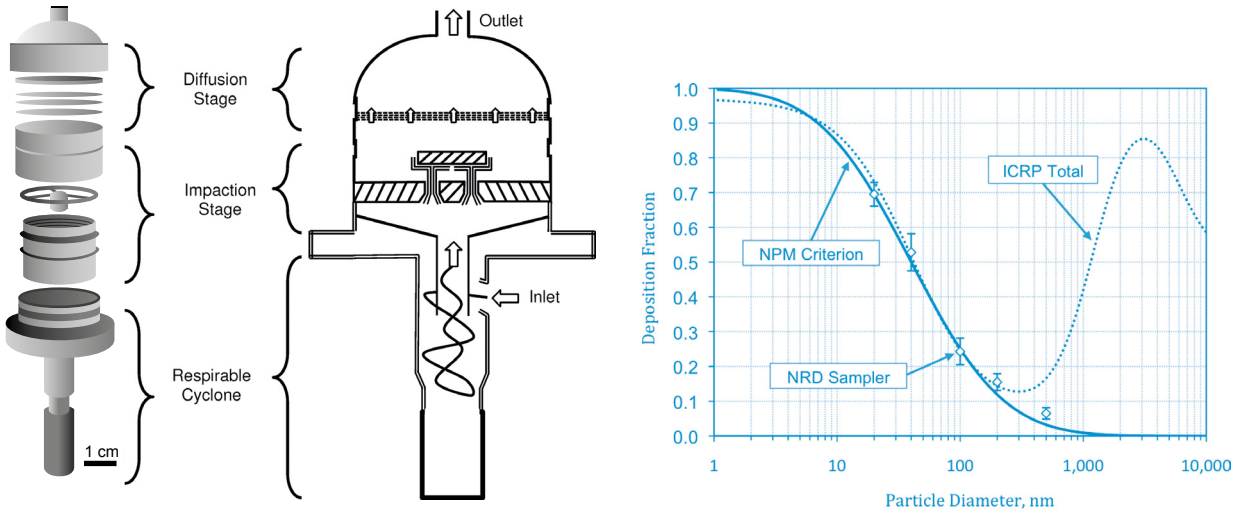


FIGURE 9: Schematic of the NRD (left); NPM sampling criterion, ICRP total respiratory deposition and effective deposition on the diffusion stage of the NRD sampler (right) [16].

[2] This information refers to the 2013 version of the instrument. The newest version (2015) of the NANOBADGE is quieter.

The sampler consists of a respirable aluminium cyclone used to eliminate particles larger than 4 µm, followed by an impaction plate where particles larger than 300 nm are collected and a diffusion stage containing eight hydrophilic nylon mesh screens with 11 µm pore size and 6 % porosity that collect particles with an efficiency that matches the NPM criterion.

The particles collected on the nylon fibers of the mesh screens can be characterised either by chemical analysis or by scanning electron microscopy to determine the size, number and chemical composition of the collected particles. The NRD sampler has not been available to the nanoIndEx project and is therefore not further covered in this Guidance Document.

2.3.1.4. Prototypes personal samplers

A variety of developments of personal nanoparticle samplers can be found in the scientific literature. Two of them have been available in nanoIndEx and are hence exemplarily presented here, namely the $PM_{0.1}$ personal sampler (PNS) [17] and the personal nanoparticle sampler (PENS) [18].

The $PM_{0.1}$ personal sampler consists of a commercially available two-stage pre-cut impactor used to remove particles in the micron size range ($PM_{1.4}$-TSP), followed by a pre-cut inertial filter that uses webbed stainless steel (SUS-316L) fibers to remove fine particles ($PM_{0.5}$–$PM_{1.4}$) and a layered mesh inertial filter used for the $PM_{0.1}$ separation. The layered mesh inertial filter consists of commercially available mesh copper TEM grids sandwiched between copper spacers and has the advantage that these provide a uniform structure of fibers aligned perpendicular to the flow direction, maximising the inertial effect on particles with less pressure drop and no loss in separation performance. By immersing the TEM grids in an appropriate solution, the collected particles can be extracted for chemical analysis.

The Personal Nanoparticle Sampler (PENS) enables the collection of both respirable particulate mass (RPM) and nanoparticles simultaneously at a flow rate of 2 L/min. It consists of a respirable cyclone, used to remove particles larger than 4 µm in aerodynamic diameter, a micro-orifice impactor with a cut-off diameter of 100 nm and a filter cassette containing a 37 mm Teflon filter. The micro-orifice impactor consists of a fixed micro-orifice plate with 137 nozzles of 55 µm inner diameter and a silicone oil-coated Teflon filter substrate rotating at 1 rpm to achieve a uniform particle deposition and avoid solid particle bouncing. Particles ranging from 4 µm down to 100 nm are collected on the impaction plate of the micro-orifice impactor, while nanoparticles are collected on the filter of the final stage, although at a rather high pressure drop 14 kPa.

2.3.2. Samplers for electron microscopic analysis

2.3.2.1. ESPnano

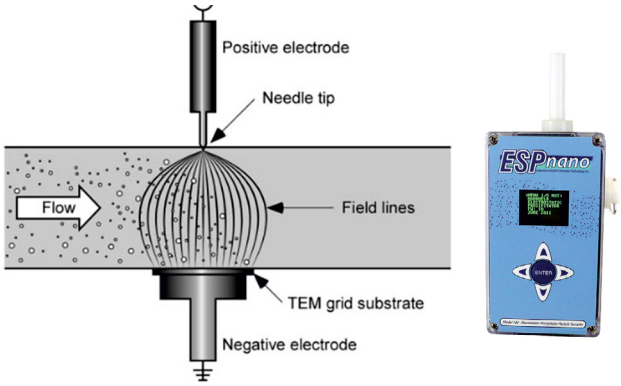


FIGURE 10: Schematic (left) and photograph (right) of ESPnano 100. [20]

The commercial handheld electrostatic precipitator (ESP) is available from ESPnano (model 100, ESPnano, Spokane, WA, USA). [19] This sampler is small and battery operated and collects airborne particles onto TEM grids. A schematic of the ESP is shown in Figure 10. The sampler is intended to be used mainly in workplace exposure assessment to take samples in locations, where a release of particles is suspected. The TEM analysis can then provide proof for the presence or absence of certain substances. The sampler is, however, handheld and not personal.

The ESPnano model 100 uses a unipolar corona charger to generate ions near a tip electro-

de. When a positive high voltage is applied to the tip, a corona is formed that ionises the air. The tip electrode faces the sampling electrode with the TEM grid. Consequently, the generated ions follow the electric field lines into the perpendicular aerosol flow, where they collide with the particles to charge them. The charged particles are deposited onto the TEM grid within the same electric field that is used to generate the ions and charge the particles. As the device is intended to be used under field conditions a removable "key" system was designed that would insure a fast and easy replacement of the sample media between different samplings. The sample media can be pre-loaded in the lab onto the key and after sample collection the key can be kept in airtight holders until the sample analysis are performed.

2.3.2.2. Thermal Precipitator Sampler (TPS)

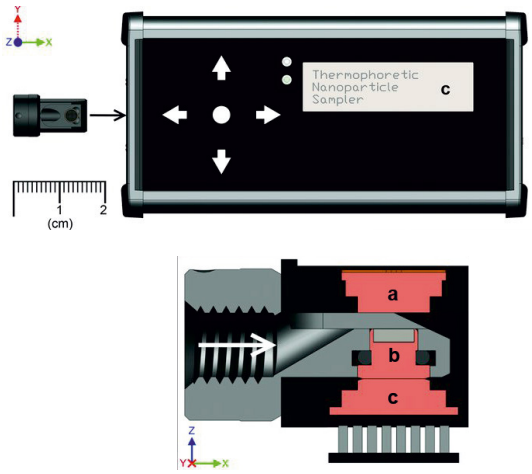


FIGURE 11: The thermal precipitation sampler (TPS): the overall device including the removable sample cartridge (top); bottom: view of the TPS region containing the hot plate (a), TEM grid holder (b) and cold plate (c). [21]

The Thermal Precipitator Sampler (TPS, RJ Lee Group, Monroeville, PA, USA) uses the thermophoretic force to collect nanoparticles onto standard TEM grids, for subsequent analysis of particle size, concentration and chemical composition. It is thus not a mass sampler. The sampler collects airborne particles by applying a relatively large temperature gradient to a narrow flow channel. Because of the temperature gradient, gas molecules on the hotter side of the particle have greater kinetic energy than those on the colder side, transferring more net momentum per collision to the particle than do molecules on the colder side, causing a thermophoretic particle motion. The particles will move in the direction of decreasing temperature and will eventually deposit onto the colder side of the flow channel that includes the TEM grid.

The TPS samples aerosol at a flow rate between 1 and 10 mL/min and utilises a removable sample cartridge that holds a hole-free carbon film supported by a 200 mesh nickel TEM grid onto which particles are deposited. The cartridge can be slid into the TPS body for sampling immediately below the hot plate while maintaining thermal contact with the cold plate to establish the thermophoresis zone (see Figure 11). Because nickel is ferromagnetic, the grid is held in place by a small magnet located between the cold plate and the grid itself.

A transfer function was developed that relates the number, size and composition of the collected particles to the ones of the test aerosol in order to reconstruct the particle number size distribution. [21] The TPS has not been available during the nanoIndEx project and is therefore not further covered in this Guidance Document.

2.3.3. Specific case of carbon-based aerosols

The service to provide a quantification of carbon-based aerosols was not fully operational in 2013– 2015 for the NANOBADGE sampler. Therefore, during the project the NANOBADGE cassette was adapted (prototyping) to allow sampling carbon-based aerosols on quartz filter for subsequent analysis in a thermal-optical analyser [22] (Lab OC-EC Aerosol Analyser from Sunset Laboratory). Soot particles were generated by spark generator and by diesel engines and were successfully collected by the sampler on freshly fired quartz filters. The mass of elemental carbon deposited on the filters has been determined

by thermal-optical analysis. The low mass of elemental carbon on the filter, combined with contamination by organic compounds when mounting the filters, made it difficult to draw reliable conclusions on the results obtained. Nevertheless, a proof-of-concept has been obtained and the preliminary results suggested that with some technical improvements (e.g. new ways to mount the filters and to sample a representative piece of filter, etc) the NANOBADGE sampler could provide quantitative analysis of elemental carbon ("black" carbon). In 2016, new sampling cassettes were proposed for the NANOBADGE sampler but they were not available during the nanoIndEx project to be evaluated and further covered in this Guidance Document.

2.3.4. Accuracy and comparability of the personal samplers

2.3.4.1. PGP-FAP

The filtration efficiency of the membranes used in the PGP-FAP (see Table 2) was estimated to be 99.8 % by connecting a Nanometer Aerosol Sampler (NAS, TSI model 3089) [23] downstream of the filter and evaluating them by SEM. Collected particles were characterised, classified and counted with respect to their morphology. Due to the high collecting filter area of 707 mm^2, in principle very low nanofibre concentrations can be detected. However, this requires acquiring a sufficient number of SEM images. The German concentration threshold for clearance measurement of less than 1000 fibres/m^3 can for instance be tested by evaluating a filter area that has collected the particles of 2 litres aerosol. After a collection time of 8 h at 2 l/min flow, a filter area of 0.74 mm^2 needs to be analysed to test for fibre clearance. The number of SEM images to map this area depends on the characteristic structure size of the particle or fibres to be counted. As a rule of thumb for the detection of fibres, the pixel resolution of an SEM image should correspond to the diameter of the fibres to be counted. If very thin nanofibres need to be detected and counted however, the required pixel size, i.e., high magnification can lead to an enormous amount of SEM images.

2.3.4.2. NANOBADGE

The NANOBADGE filters are analysed by X-ray fluorescence spectroscopy (XRF) providing a cumulative mass-based quantification of the chemical elements present on the filters. Thus, the sampler provides the mass concentration in the breathing zone averaged over the total sampling time. The quantification by mass of the elements deposited on the filters requires that the XRF spectrometer is calibrated, which was done using a previously reported methodology. [24] In short, sets of filters of increasing particle loading are generated by sampling controlled aerosols (e.g. ZnO, TiO_2, etc.). The filters are then analysed by XRF, followed by dissolution of the particles for elemental quantification by ICP-MS. The plot of the normalised XRF intensity versus the mass determined by ICP-MS yields the calibration curves for the different elements studied. These are used to convert the X-ray fluorescence intensity to mass. The limits of detection (LOD) for the following elements have been determined for the NANO INSPECT XRF as shown in Table 3.

	LOD (ng/filter)
Al	100.2
Si	20.1
Ti	2.6
Ca	6.8
Zn	1.5

TABLE 3: Limits of detection of the NANOBADGE using XRF analysis (NANO INSPECT XRF, optimised Z offset, 0.1° angle, 200 sec acquisition).

To further illustrate the validity of the sampler for personal exposure assessments, the level of detection (LOD) for ZnO and TiO_2 have been determined using another instrument, the Rigaku NANOHUNTER XRF that was used at CEA for the project nanoIndEx. [25] The European Agency for Safety and Health at Work distinguishes long-term and acute exposure, the former being a repeated exposure averaged over working shifts of 8 h and the latter a peak exposure averaged over 15 min. [26] Thus, the LODs have been converted to aerosol mass concentrations for a full shift based on the

latest recommended exposure levels (REL) of the National Institute for Occupational Safety and Health (NIOSH). [27] The minimum sampling time required to detect an exposure at or above the REL has been calculated. As shown in Table 4, the limits of detection are much lower than the REL for the two oxides considered in this study. The detection of peak exposure is also possible, since a few seconds of sampling at or above the REL are sufficient to exceed the LOD. Since the LOD are several orders of magnitude smaller than the current REL, the NANOBADGE sampler can already accommodate tougher regulation, should the exposure levels be lowered in the future.

The highly sensitive XRF technique yields the elemental composition of the collected particles with sensitivity in the order of a few tens of nanograms per filter. Cconsequently, it could be used either over a full shift (e.g. 8 h) or during short operations (e.g. 15 min) to detect acute exposure events. The main drawback observed is that the sensitivity of this analytical technique is decreasing dramatically for light elements (Z < 13) and therefore carbon-based particles cannot be analysed with this technique.

	REL for ultrafine dust from NIOSH (µg/m³)	**LOD** (ng/filter)	**LOD** (µg/m³) **for 8 h of sampling**	**Minimum sampling time at the REL**
ZnO	5000	30 ±20%	0.1 ±25%	< 1 min
TiO_2	300	12 ±25%	0.04 ±30%	< 1 min

TABLE 4: Comparison between the recommended exposure levels (REL) published by the NIOSH and the limits of detection (LOD) of the NANOBADGE sampler for shift and acute exposure (Rigaku NANOHU TER XRF, optimised Z offset, 0.75° angle, 200 sec acquisition).

Several measurement campaigns were organised during the course of the project at IUTA, IGF and CEA on monodisperse, polydisperse, compact, and agglomerated particles. Those measurements allowed us to evaluate the NANOBADGE sampler in various conditions with different aerosols (size distribution, morphology, chemical composition, etc.) and against different granulometers, counters and monitors.

The example shown in Figure 12 illustrates the performance of the NANOBADGE compared to a scanning mobility particle sizer (SMPS) by carrying out simultaneous measurements on test aerosols of ZnO. The effective density and shape of the particles present in the test aerosols were determined experimentally using a tandem DMA-ELPI setup [28] to compare number-based data obtained with the SMPS with mass-based data obtained with the NANOBADGE.

The sampler has been evaluated and validated up to a size of 200 nm using several aerosols of ZnO and TiO_2 particles. The agreement between the SMPS and the NANOBADGE sampler was within ± 25 % on all test aerosols for which the effective density was determined (see Figure 12).

This study highlights the fact that the density of the particles in aerosols is of great importance to compare electrical-mobility-based results to mass-based measurements. When aerosols are monodisperse with perfectly spherical non-agglomerated particles, results from SMPS and CPC might be easily converted to mass. However, in case of more complex aerosols (i.e. polydisperse or agglomerated), the effective density of the agglomerates has to be precisely known in order to reduce the deviation between monitors and samplers. Therefore, metric conversion has not been performed on data generated during field measurements. Qualitative evaluation of events, from direct reading instruments and cumulative mass-based quantification of the chemical elements present on the NANOBADGE filters, could be of high value for the occupational exposure assessment.

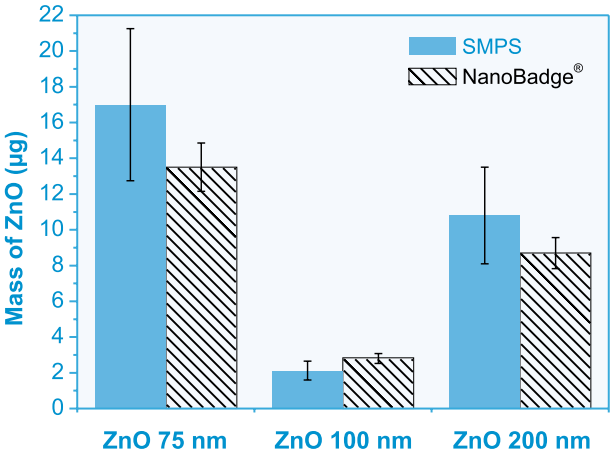


FIGURE 12: Mass of ZnO calculated from the SMPS data and mass of ZnO measured by XRF analysis of the NANOBADGE filters (calculated from the mass of Zn). An effective density of 2.2 g/cm³ was used.

2.4. Periphery

2.4.1. Sampling tubes

A personal sampler or monitor can only be mounted directly in the breathing zone, if it is sufficiently small and lightweight. Otherwise, the instrument can be fixed on a belt to sample from the breathing zone via flexible tubing. These tubes can introduce artefacts that bias the measurement. Particle losses are unavoidable during aerosol transport. These losses are mainly driven by particle diffusion, sedimentation, and inertial and/or electrostatic deposition. Sedimentation and inertial losses are typically negligible in case of nanoparticles due to their low mass, but diffusion losses increase with decreasing particle size and with increasing residence time inside the tube of a given diameter. Therefore, sampling tubes should be kept as short as possible. In order to avoid electrostatic particle losses, the tubes used should generate no electrostatic charges or electric fields. This is best achieved by the use of electrically conductive tubing. For this purpose, carbon impregnated silicone tubes are very commonly considered as the optimal choice in aerosol measurements. However, it was found previously, that siloxanes might degas particularly from new silicone tubes [29]. These siloxanes can be adsorbed by particles and alter their chemical composition [30]. Furthermore, they form a silicon oxide deposit on the electrodes of a corona charger [31] that may affect the charging efficiency [32].

During the project, we found that besides the adverse effect on the corona electrode, siloxanes in the gas phase are preferentially ionised in corona chargers, like the ones used in DiSCmini, Partector or NanoTracer. Siloxanes are very large and heavy molecules and thus the ion properties in the charger change drastically, resulting in a decreased particle charging efficiency. We found that especially the DiSCmini significantly underreports the particle concentrations, when sampling through (new) conductive silicone tubes [33]. The discrepancy can reach a factor of two or more in case of the DiSCmini/miniDiSC, but are much lower for the partector (see Figure 13).

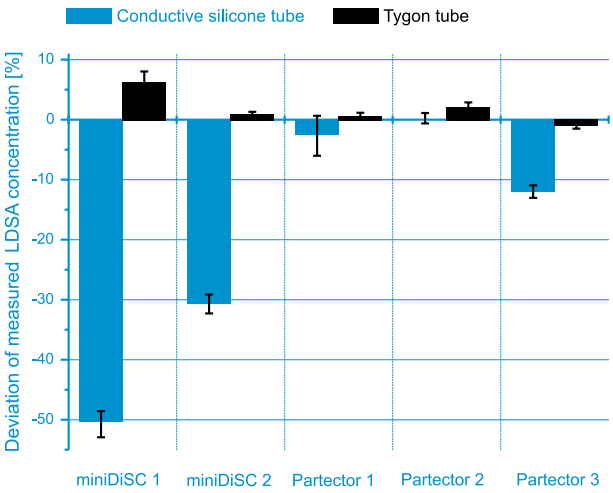


FIGURE 13: Deviation of LDSA concentrations measured with miniDiSC and partector caused by conductive silicone tubing [34] and Tygon® tubing [35].

During comparison between different sampling tube materials, the lowest discrepancy was expectedly found with stainless steel tubes. However, these are not flexible and can hence not be used in personal measurements. Tygon® tubes were found to be the best compromise between low measurement artefacts and good practicability. This is in good agreement with work done in the 1980's [36] when conductive tubing was not yet available. If sampling tubes are needed in personal exposure measurements, the use of Tygon® tubes is therefore recommended. In case of personal samplers, the sampling

head is usually mounted at or near the collar bone of the individual, while the pump that generates the sampling flow rate rests on the belt. Flexible tubes are used to connect the pump and the sampling head. As long as the sampling substrate (e.g. filter) resides inside the sampling head, the choice of tube material does not play a role. If, however, the particles to be sampled are transported through a tube, caution should be taken to assure low losses inside and low degassing from the material. Degassed molecules may be adsorbed on the particles' surfaces and change their chemical composition.

Hence it is recommended, not to use any silicone tubes to transport the aerosol in measurements involving unipolar diffusion chargers or samplers used for subsequent chemical speciation. The use of Tygon® tubing currently seems to be the best compromise.

2.4.2. Pre-separators

Inertial pre-separators such as impactors or cyclones are commonly used in aerosol measurements in order to limit the particle size range. Such pre-separators remove all particles that are larger than the so-called cut-off size of the preseparator. They are used to adjust the particle size range of the aerosol either to match a certain sampling convention, e.g. particles < 4 µm (d_{50}) in case of the respirable fraction or to limit the particle sizes to the measurement range of the instruments. In dusty workplace atmospheres, such pre-separators are also helpful in protecting the instruments. Limitation of the aerosol to the measuring range of the instrument is of particular importance for some of the personal monitors. The monitors are designed to measure the number and/or lung deposited surface area (LDSA) concentration of the airborne particles. As described above, measurements with reasonable accuracy are only possible for a limited size range. A pre-separator with 400 nm cut-off would for example be required for accurate LDSA measurements, which as of now is not commercially available.

2.4.3. Personal pumps

Most personal (filter) samplers require the use of a personal, battery-operated pump in order to draw the required flow rate through the sampler. In principle, a pump should be chosen to provide the necessary flow rate, taking into consideration the pressure drop of the sampler. Novel nanospecific samplers with cut-off sizes in the nanometre range exhibit a higher-pressure drop than classic e.g. respirable cyclones, thus necessitating stronger pumps. Another important issue to take into consideration when choosing a pump for nanospecific samplers, is that the higher-pressure drop increases the battery consumption, i.e. the battery lifetime is significantly reduced. During the nanoIndEx project, it was found that pump batteries, designed for > 8 h continuous operation with conventional samplers were already discharged after only around 4 h when used to sample with (prototypes) of samplers with 100 nm cut-size.

2.5. Field applicability of personal samplers and monitors

Instruments intended to assess individual exposure of workers to MNMs in the field need to satisfy a number of specific requirements. Basic aspects address portability and include battery operation time, robustness and wearability during regular work as well as aspects of mechanical, electrical and explosion safety. Furthermore, the instruments have to produce reliable results not only under laboratory conditions, but also when carried by a person in the field. The usability of instruments for daily assessment depends predominantly on its weight and bulkiness. Since a minimum of 8 h battery life is necessary to collect data over a full work shift, battery capacity can be a significant weight and volume factor of portable instruments. Therefore, measurement principles with high-energy consumption may not be appropriate for personal application.

2.5.1. Practical considerations

To determine personal inhalation exposure, the inlet of the instrument must be fixed reliably in the worker's breathing zone. High weight and volume impedes direct positioning of the instrument in the breathing zone without restricting the worker's mobility. If a tube extension of the inlet must be used to allow wearing a bulky or heavy device at the belt or in a backpack, careful selection of appropriate tube materials becomes necessary together with estimation of associated wall losses inside of the tube. As described in section 2.4.1, degassing of siloxanes from silicone tubing can significantly affect the measurement accuracy of some diffusion charging instruments and may also alter the particles' chemical composition. In very dusty environments, impactors or cyclones used for limiting the particle size range and/or for protection of the instrument may clog and require periodic cleaning. In addition, the calibration needs to be checked periodically by comparing the results from several instruments.

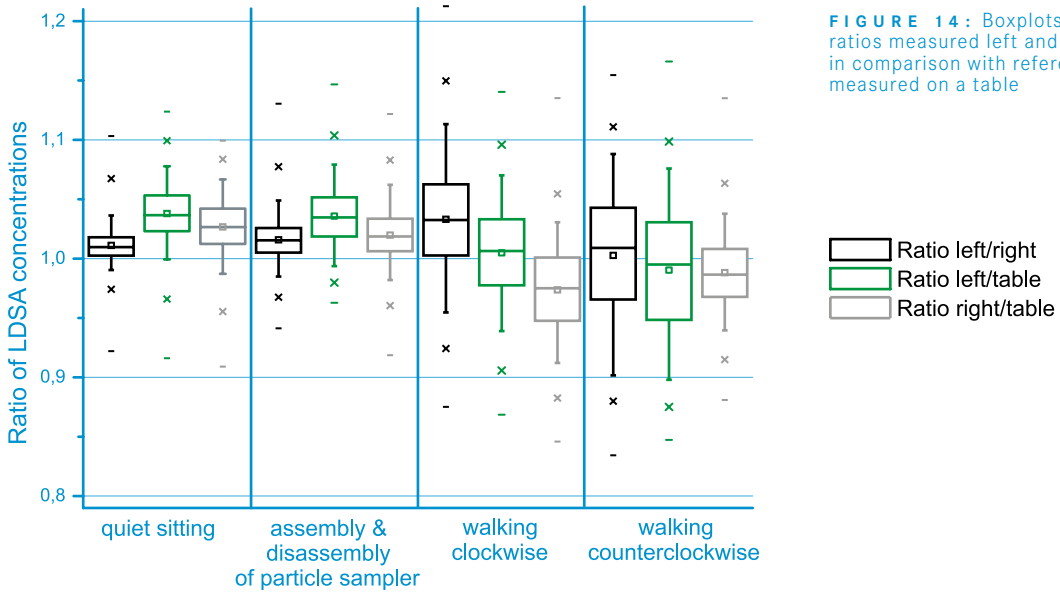


FIGURE 14: Boxplots of LDSA concentration ratios measured left and right in the PBZ and in comparison with reference concentrations measured on a table

2.5.2. Effects of wearing the instruments

The quality of personal exposure measurements may also be affected by the mode of wearing the instruments. Potential influences may stem from a variety of factors, including personal activities, vibration, local airflows or relative velocities between the person carrying the instrument and the aerosol to be measured. Such effects have been observed in numerical studies [37] and during measurements of exposure to micron particles [38]. In nanoIndEx, we conducted measurements of personal exposure to well controlled NaCl nanoparticle concentrations. During the measurements, an individual was inside a 23 m³ chamber, which was homogenously filled with the test aerosol. The individual carried two partector in the PBZ, one left and one right, while carrying out certain activities. A third partector measured while resting on a table inside the chamber. No significant differences between the results obtained from the left and right side of the breathing zone was observed. The personal results also agreed within ± 10 % with those obtained by the instrument resting on the table. However, it was noted that the data showed higher fluctuations during activities like walking than during quiet sitting, but the average was unaffected (see Figure 14). This effect is not unexpected, as walking may disturb the local flow and particle distribution, leading to short lived differences. In the experiments, this effect was purely random and therefore only affected single data points, but not the mean concentrations. The same experiments were repeated after swapping

the instruments left and right (data not shown here). In that case, the ratios reversed, i.e. the (small) differences stem from the instruments themselves, but not from the positioning of the instruments in the breathing zone. It is expected that these findings also apply to other monitors and samplers, at least as long as the sampling flow rates are similar.

2.5.3. Is the available instrumentation applicable to field studies?

The commercially available personal instruments studied in the project nanoIndEx included partector, partector TEM, NANOBADGE, MicroAeth AE51, FAP-PGP, DiSCmini, ESPnano and PUFP C100. They all satisfy the basic requirements of wearability that were discussed above and showed good field applicability. DiSCmini, ESPnano and PUFP C100 require additional tube extensions to measure in the worker's breathing zone. Selection of appropriate tubes requires care and needs to be documented (see 2.4.1). For prototype samplers like PNS and PENS that have cut-off diameters in the nanometre range and hence have a high-pressure drop, the pump operation time did not always cover a full shift's duration of 8 h. It was shown that wearing of the instruments does not affect the measurement accuracy, but it may cause a larger scatter of the data in case of measurements with high time resolution.

The currently commercially available range of instruments does not allow personal surveillance of compliance to mass based MNM exposure limits in an easy way. Only in exposure situations where MNM of clear chemical or morphological signature are being handled, filter based sampling with subsequent analysis can provide estimates of MNM-specific mass or fibre number concentrations. Examples are XRF-based quantification of MNM made from low-background elements and SEM-based individual fibre counting.

To conclude, the available instruments are technically mature and reliably useable in field measurements of personal exposure to airborne nanomaterials. Each of the instruments has its advantages and disadvantages. Data can be measured both with high time resolution or as time weighted (e.g. shift based) averages. A variety of exposure metrics can be determined. Their applicability to legislative standards is yet unclear as there is no official guidance on which metric should be used to express exposure to airborne nanomaterials measured both with high time resolution or as time weighted (e.g. shift based) averages. A variety of exposure metrics can be determined. Their applicability to legislative standards is yet unclear as there is no official guidance on which metric should be used to express exposure to airborne nanomaterials.

Chapter 3

Performance of measurements

3.1. Description and selection of the assessment task

3.1.1. Epidemiological studies

Epidemiological studies with respect to nano-objects and their agglomerates and aggregates (NOAA), try to establish dose response relationships for NOAA and selected medical endpoints. Whereas the latter aspects are not within the scope of this Guidance Document, the accurate measurement and documentation of NOAA-doses within the selected group of workers and their work life (or a selected period within that work life) need to fulfil certain pre-requisites (for general aspects of exposure assessment within epi-studies see e.g. ref. [39] with the example of crystalline silica). As a general principle, all parameters for the intended measurements ("protocol") need to be discussed with the epidemiological scientists as they will in almost all cases be a compromise between the epidemiologically wanted and the analytically possible. At first, the exact airborne component(s) to be investigated need(s) to be defined. This includes the choice of the metric to be used for the airborne particles. As normally a dose is the target of exposure assessment within epi-studies, additionally the time periods (periods of actual sampling) over which exposure has to be quantified need to be defined as well. For many epidemiological studies a so called Job Exposure Matrix (JEM) will be the final outcome of exposure assessment. A JEM assigns average exposure levels to job titles by calendar period. Based on a thorough structural evaluation of the workplaces in question job titles (i.e. jobs for which homogenous exposure levels can be reasonably assumed) need to be defined. For these job titles, typically average shift exposure needs to be determined. Normally the averaging time is 8 h, but significant deviations are possible. The sum of shift doses over the work period in question allows for calculation of the respective dose. In cases where the exposure pattern is very inhomogeneous, for example because NOAA-exposure only happens during very short time periods during a shift, it may additionally be necessary to determine the average short term exposure concentration during these episodes of potentially high exposure. As dose calculation will also be of concern in those cases, a common time base for short-term measurements should also be defined. For this purpose, a time base of 15 min is recommended, even if the episodes are significantly shorter.

3.1.2. Exposure assessment within risk assessment/risk management procedures

This document deals with exposure assessment within risk assessment/risk management procedures. In cases where occupational exposure limits (OELs) for NOAA are existing, exposure assessment strategy etc. will have to be performed according to national standards and possibly EN 689. Specific directions for these cases can be found in this standard.

Generally the question to be answered in the described types of exposure assessment (risk assessment/risk management) will be: "Are the current measures taken in risk management sufficient to minimise worker's risk for negative health effects by exposure against NOAA?" For this purpose, a first consideration must be given to the hazard resulting from a specific NOAA, i.e. its toxicity. In order to give a valid estimation of risk the current state of development of personal monitors does not allow for their use in exposure assessment of highly toxic NOAA. A possible example of this class of substances might be some specific carbon nano tubes (CNTs), i.e. long and rigid ones [40].

Person carried instruments can be used for direct and on-line number concentration or lung deposited surface area concentration measurements ("monitoring", see section 2.2). In addition different person carried instruments can be used for sampling the NOAA in question and to subsequently analyse these samples with appropriate (wet-)chemical or instrumental methods like XRF, ICP-MS or electron microscopy ("sampling", see section 2.3). The latter, i.e. the qualitative identification of NOAA in

airborne state, is mandatory, if direct reading instruments cannot sufficiently differentiate between NOAA-concentration and the respective background, which frequently will be the case. In order to answer the central question of sufficiency of risk management measures and to optimise the use of the available resources, quite often the use of a so-called tiered approach [41] is advisable. This means that in a first step the relevance of exposure assessment is checked by evaluating possible exposure using available documents and pre-knowledge of the workplaces in question (tier 1). If relevance cannot be denied, the second tier of exposure assessment will be necessary, which involves simple, fast and sufficiently reliable measurements. Personal monitors are especially useful in this context (tier 2 or "basic assessment"), although they are not explicitly included in the approach. The use of personal samplers may increase the reliability of their results by helping to clearly identify the presence of the NOAA in question.

Results of these tier 2 measurements can be:

a. **Exposure assessment was inconclusive:** Insufficient information on the nature/quantity of the risk is available/was obtained. In that case, a so-called "expert assessment" or tier 3 assessment will be necessary with much more elaborate equipment and effort. Person carried instruments MAY be part of tier 3 measurements, but will not be sufficient in most cases.
b. **Exposure assessment was conclusive – risk management measurements are not sufficient:** In that case, additional measures have to be implemented and subsequently exposure assessment has to be repeated.
c. **Exposure assessment was conclusive – risk management measurements are sufficient:** In that case, the outcome of the exposure assessment has to be documented and the normal repetition cycle of risk assessment procedures entered in the particular company.

The most important task when choosing a tiered approach is to define decision criteria, which allow for one of the above mentioned cases to be identified. Examples for these are given in [41].

3.2. Selection of the measurement devices

3.2.1. Epidemiological studies

Depending on the outcome of the description and selection of the assessment, task (see above), suitable measurement equipment needs to be selected. Availability of procedures and equipment will almost certainly have already been a major topic in the above mentioned discussion and selection process. However, devices and measurement/sampling procedures should at this point be selected from the available (chapters 2.2 and 2.3) and suitable (chapter 2.4) instrumentation with a clear view of the above-discussed parameters. This must also include practical considerations like the need for use of explosion proof equipment or possible sampling time restrictions in battery-powered equipment with respect of the need of covering shift exposure.

Personal sampling should in doubt be selected instead of static sampling, although both can have an added value. Shift exposure should preferably be measured by direct coverage of the whole shift. However, it may also be calculated from time weighted averaging of distinctly different periods of exposure periods within a shift, if more practical e.g.: selectivity, sensitivity and further quality parameters of the selected equipment/procedures need to be covered as well.

3.2.2. Exposure assessment within risk assessment/risk management procedures

Which personal monitor or sampler is chosen depends on the specific workplaces and NOAA in question. The diffusion charger type instruments are robust and widely applicable; however, their limitations at particle diameters above 400 nm should be taken into account. [14] If the workplace exposure will be characterised

by significant agglomeration/aggregation of the primary nanoparticles, larger particle sizes need to be taken into account. This will actually regularly be the case. Optical instruments (photometers, optical particle counters) may additionally be used then to cover the particle size range of 300 nm to a few µm (i.e. the respirable dust).

The selection of personal samplers will mainly be ruled by the intended subsequent analysis. So chemical analysis like XRF or ICP-MS will require a minimum of particle mass to be sampled (LOD) with a filter. XRF and SEM analyses require the particles to be deposited on a flat surface of e.g. a track-etched membrane filter. Alternatively, transmission electron microscopy (TEM) and subsequent elementary analysis will require specific sampling media (see 2.3).

Selection of the proper monitors and samplers is crucial for the success of exposure assessment and needs to be done with respect of conditions in the workplace (like work pattern, suspected concentration range, nature of background, NOAA in question etc.) and should be well documented (see below).

3.3. Selection of the workplaces or emission sources to be investigated

3.3.1. Epidemiological studies

From the job title selection process described in section 3.1.1, at this point the general types of workplaces to be covered are already known. For epidemiological studies, emission measurements are normally not suited.

For all workplace types (job titles) to be covered, at this point a detailed discussion of the exposure determinants, i.e. all the parameters influencing the height of exposure during a given shift, need to be discussed and documented (see for example TRGS 402 [42]). The results of exposure assessment for each job title need to be representative for that job title and the respective calendar time period of the JEM (see above).

3.3.2. Exposure assessment within risk assessment/risk management procedures

Once the equipment (monitors, samplers, sampling media etc.) has been chosen it has to be decided whether emission or exposure concentrations will be better suited to answer the central risk management question.

Generally, the respective concentrations will have to be determined with and without the specific control measures (technical, organisational, personal in that order of relevance) in place. The most important obstacle to unambiguous results of these measurements will be large and fluctuating background concentrations in the same metric as chosen for the monitoring exposure assessment. Therefore, recording continuously (or at least quasi-continuously) of the concentrations and comparison with a detailed “diary of events” (log) over the course of measurements is a very useful approach in order to identify non-work related episodes/events influencing the exposure/emission concentration and the background alike. [43] Additionally, qualitative identification of the NOAA in question by suitable analyses of the samples (see above) will be necessary in most cases. In many cases, grouping of the investigated workplaces into so-called source domains [44] will also be helpful.

Time base of the measurements will largely be ruled by the time characteristics of the task in question. Therefore, short activities (e.g. emptying of a container of nanomaterials or cleaning of a small production site) should be accompanied by monitoring during these activities. There is a certain conflict between monitoring and sampling if very short activities are to be investigated, as limits of detection of certain analytical methods may require longer sampling times than monitoring periods. In fact, sometimes sampled mass may simply not be adequate for these types of analyses. In the latter cases, repletion of tasks and sampling

onto identical sampling media may be a way out of this problem.

NOTE: For comparison of the measured exposure concentrations with an existing OEL shift measurements/sampling and additionally short-term measurement/sampling (15 min recommended) may be required additionally.

3.4. Background management

3.4.1. Epidemiological studies and risk assessment/risk management procedures

As background treatment and its description is more or less identical for epidemiological and risk related studies we do not describe them separately.

Depending on the nature of the component (NOAA) to be determined, the procedure for background treatment needs to be discussed beforehand.

The epidemiological study in question may not be interested in the discrimination of urban background particles from the ones resulting from workplace activities, depending on the medical endpoint to be determined. If that is the case (e.g. because unspecific response of the airways to ultrafine particles within a specified size range is the selected endpoint), no further separate treatment of the background may be necessary.

In many cases, however, the study in question will be interested in specific NOAA workplace exposure and in those cases the omnipresent, non-workplace related background of ultrafine particles must be properly addressed and treated. How well this is done will determine the quality of the study in a major way. The following possibilities exist:

- Specific measurement of ONLY the NOAA in question with direct discrimination of the background (e.g. chemical or morphological speciation)
- Spatial compensation of the background by measurement close to the workplace in question (during activities) and away from it (“Near field”, “Far field”)
- Temporal compensation by measuring with and without the specific activities of the workplace
- A combination of the latter two

In addition, special consideration should be given to the “outdoor” (i.e. outside the respective building) background, which may mostly be influenced by combustion engine exhaust. The final agreed upon method of background treatment needs to be part of the protocol for the performance of exposure assessment in the respective epi-study. For risk assessment/risk management, the non-workplace related background of ultrafine particles must be properly addressed and treated as well. The same considerations as mentioned above apply as well.

Specific guidance on background treatment is given in [45].

3.5. Performance of the measurements

3.5.1. Epidemiological studies

The results of discussions and decisions as of paragraphs 3.1.1 to 3.4.1 are condensed into a final “protocol for the assessment of exposure” which is basically the standard operation procedure for that measurement campaign. All measurements shall be performed according to that protocol and documented respectively.

3.5.2. Exposure assessment within risk assessment/risk management procedures

The actual measurements shall be performed according to a pre-determined work plan (“protocol”), preferably following an existing standard operation procedure. This protocol has to describe in detail, how the tiered approach (if any) for exposure assessment is working in the respective case. Special consideration

has to be given to the decision criteria as of 3.1.2 above. Actual measurements (application of monitors and samplers) shall follow existing standard operation procedures. [46]

3.6. Data evaluation

Data treatment and evaluation is described in chapter 4 in detail.

3.7. Documentation

3.7.1. Epidemiological studies

The actual documentation is one of the core elements of the respective epidemiological study and is not further discussed here. Of course, it shall contain ALL relevant aspects discussed in this chapter.

3.7.2. Exposure assessment within risk assessment/risk management procedures

The documentation of the results has to be described in the protocol as of 3.5.2 above. It has to include

- all relevant data for the actual performance of assessment ("who, where, when"),
- decisions taken in planning of the actual measurement campaign (see above) including the decision criteria within the scope of a tiered approach (if any),
- the results of all measurements during monitoring (preferably also primary data of monitors),
- the results of averaging of the monitors' saved data during the sampling periods,
- the sampling details of monitors and samplers,
- and the results of sampling

The latter includes data for all pre-selected metrics, e.g. respirable mass concentration, mass concentration of a specific NOAA, qualitative analyses of filter samples and identified NOAA etc. A formal evaluation of the measurements/assessments with respect to and taking into account the pre-selected decision criteria of a tiered approach, if any, is mandatory. This will result in one of the possible formal outcomes described in 3.2.2.

3.8. Quality assurance

All instruments used in field studies should work as reliably and as reasonably possible. A manufacturer calibration of each instrument prior to each field study is certainly not possible due to time and financial restrictions, but the calibration of the instruments should frequently be checked by comparing them with each other. The simplest check that should be done very frequently is to measure (and adjust, if necessary) the flow rate of the instruments. Another rather simple check of the instruments' calibration is to let several instruments run side by side over a certain time. Results should be compared and each data set should be checked for any obvious anomalies. This simple test should be performed prior to each measurement campaign, ideally upon arrival at the workplace, because of potential damages during the transportation of the instruments to the site.

More elaborate round robin tests using well defined test aerosols as e. g. carried out by Kaminski et al. [47] should also be carried out periodically to elaborate on the limits of the instruments' comparability and assure that instruments are also comparable with the ones from other institutions.

Chapter 4

Data collection, analysis and storage

4.1. Data collection

In carrying out field studies, it is important to consider how the relevant data should be collected. In order to allow for appropriate analysis and interpretation of the data obtained from the measurement equipment, contextual information should also be collected. This contextual information should include a number of vital pieces of information:

- A description of the task(s) that are being carried out during the measurement period
- The position of the samplers and monitors, on people and in the room. Including identification of movement of any of the instruments (i.e. moving from near field to far field)
- Information on any events that occurred during the measurement period
  - Relevant to the equipment such as period of cleaning
  - Relevant to the task such as emptying of bag of particles
  - Relevant to activity in the room (or outside) such as opening windows
- Information on the nanomaterials being used in the process
  - Type of material, size, density, morphology
- Information on the room
  - Room dimensions
  - Ventilation

A database structure has been developed by the PEROSH group with the aim of enabling collection of measurement data in a harmonised format. This database is called NECID (Nano Exposure and Contextual Information Database) [48]. The NECID database has been designed to store all available contextual information for a measurement series and therefore includes tables on the workplace itself, the materials, tasks carried out, other sources of emission, availability of general and local controls, the workers, their experience and use of PPE. At the time of planning the nanoIndEx field studies, the NECID database was only available to partners in the PEROSH group and two consortium members who had been granted permission to use it. Not all partners in nanoIndEx had access to NECID and so to facilitate the data collection for storage in NECID excel templates were developed, based on NECID[3]. An accompanying data collection protocol was also developed to assist the exposure scientist in collecting the relevant data and ensuring that the samplers/monitors were identifiable. As NECID aims to collect data on all possible aspects of the field study the templates are quite large and could potentially take some time to fill out for a specific study. Therefore a simpler template was developed to collect the contextual data essential for the data analysis so that the analysis could be undertaken without delay.

It is important to consider using a standard data collection template in field studies, particularly when conducted by multiple organisations as this will ensure that the same data are collected for all field measurements. While the NECID structure is not yet accessible to all organisations, the idea of harmonising data collection going forward will result in the potential to pool data from field studies for future work, such as investigating exposure for epidemiological studies.

4.2. Data analysis

The focus of the data analysis in nanoIndEx was to compare the measurements obtained from monitors. In particular, to compare the measurements obtained from the personal monitors to each other, and to reference monitors (stationary equipment).

4.2.1. Preliminary analysis

As with all data analysis, the first step is to visualise the data to start to form an opinion of what the statistical analysis will tell you. Time-series plots (Figure 15a) allow for a visual comparison of the entire set of data. When the main purpose is to compare measurements of

[3] These documents are available for download on the nanoIndEx webpage www.nanoindex.eu

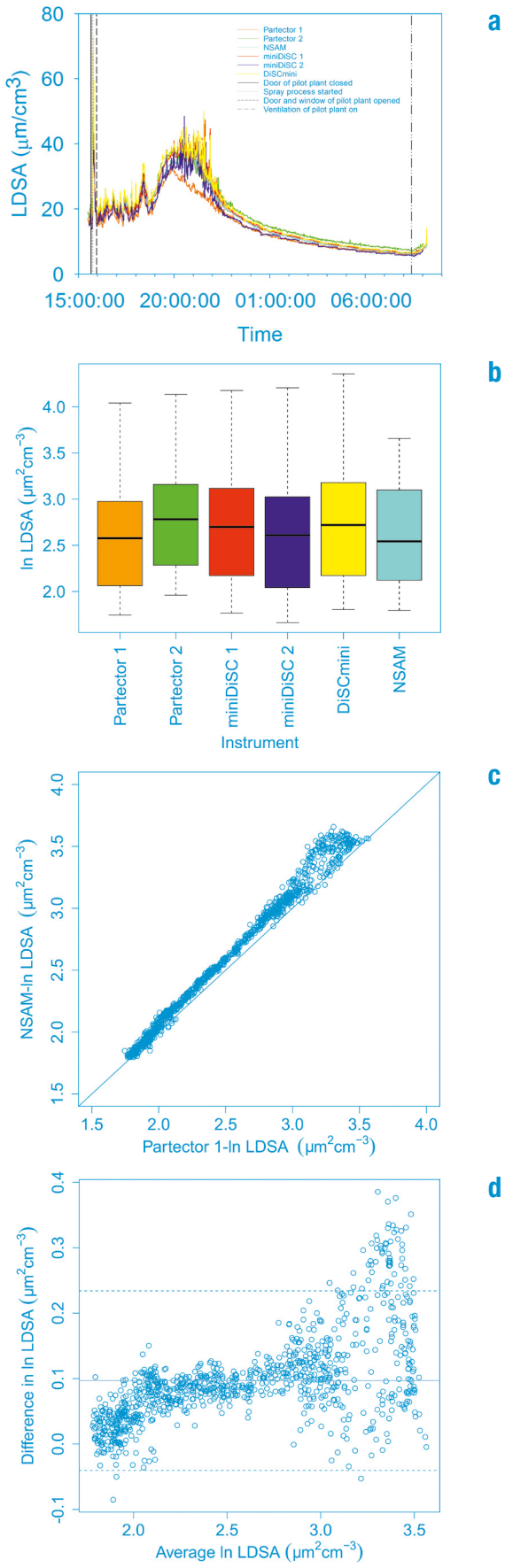


FIGURE 15: Examples for graphical representation of the measurement data, (a) time series, (b) box plot, (c) scatter plot, (d) Bland-Altman plot.

different instruments, the main things to look for are whether the monitors behave the same, do they measure exactly the same, do they move in parallel (presence of an offset), does one monitor behave differently at higher/lower concentrations, and is this behaviour consistent over the entire measurement period. The same process could be used to compare measurements taken in different positions. Time series plots are also important for identifying peaks and troughs and allow for an initial impression to made, when compared with the contextual information regarding the timings of tasks and background events, on whether they are associated with anything that has been observed and recorded during the measurement period.

Boxplots (Figure 15b) allow for an impression of the overall distribution of concentrations measured, whether one monitor has more variation than another and whether the median and range is the same. Scatterplots (Figure 15c) of the measurements obtained from two monitors should be examined to determine whether the two monitors measure exactly the same (all points lie along the line of equality), there is a consistent offset (the points lie above or below the line of equality but are parallel to it), or whether there is evidence of some other relationship between the results from the two monitors (a straight line or curve that does not follow the line of equality). A final plot that is useful when comparing two measurements is the Bland-Altman plot (Figure 15d). This plot shows the difference between measurements against the average of the two. From this plot you can see what the actual difference is between the two monitors and make some evaluation of whether this difference is important or not (i.e. a difference of 5 will be important in terms of measuring temperature, but not in terms of measuring number concentration). Looking at the plot as a whole, you can evaluate whether there is any pattern in the points, does the difference increase with increasing concentration (upwards sloping line), decrease with increasing concentration (downward sloping line) or is there some other relationship evident.

These plots and your evaluation of them will provide some impression of the relationship between two monitors.

4.2.2. Further analysis

The next stage is then to consider some numerical evaluation of whether the two sets of measurements differ and how. Generally, this would involve investigating paired differences, but in the case of time-series data there is an added complication as the data within a time-series is not independent (i.e. the value obtained at time T_i depends on the value at the previous time point T_{i-1}). Within nanoIndEx we have considered a number of methods to evaluate the difference between two time series, and attempting to take account of the dependence of the data. Initially, however, we considered some more standard measures for the comparisons.

4.2.2.1. Bias

Bias is an important measure for how close an instrument is to the true value. Often the 'true' value is not known; in this case, you can either take the reference monitor as the 'true' value or the average value of all of the instruments being compared. Often the latter is taken as the median rather than the mean to avoid the value being influenced by any outliers.

Essentially the bias is the ratio of the difference between the value obtained from the instrument, I, and the true value, T.

$$\text{Bias} = \frac{I - T}{T}$$

The bias can then be multiplied by 100 and represented as a percentage; bias of 0.2 = 20 % bias.

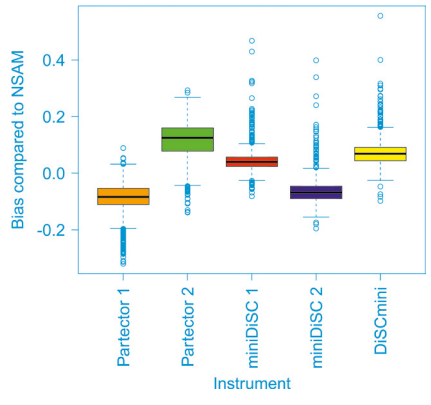


FIGURE 16: Boxplot of bias of different instruments compared to NSAM.

This can be calculated for the entire measurement period and summarised. The most straightforward way to evaluate the bias may be to present it as a boxplot (Figure 16). The range of bias can then be examined and an evaluation made about whether it falls within an acceptable range (± 30 % is usually though of of as acceptable for equipment measuring particle concentrations). The boxplot shows that the bias is within the range of ± 30 %. Two of the instruments are negatively biased, indicating that the measure consistently lower than the reference, while the others are positively biased, indicating that they measure consistently higher. The bias is lower for the miniDiSC and DiSCmini than the partector.

4.2.2.2. Precision

The precision is a measure of the variability. This can be calculated by:

$$\text{Precision} = \frac{\text{Abs}(A - {}^{A+B}/_{2})}{{}^{A+B}/_{2}}$$

Plotting the bias and precision against the time and 'true' concentration allow us to see if either of these factors has an impact on the bias and precision. Does the bias increase with increasing concentration? Does the precision decrease with increasing time? Further to this, regression models can be used to investigate whether the concentration and/or time (Figure 17) have an impact on the ratio, or the difference.

The boxplot of the precision (Figure 18) agrees with the impressions gained from the bias plots, there is more variability in the partector, in this case, and so lower precision.

4.2.2.3. Distance

Distance between two time series can be used as another measure of how similar they are. Simpler measures such as Euclidean distance, Manhattan distance and dynamic time warping are often used but these ignore the temporal aspect and serial correlations of the data.

Each of the methods uses a slightly different equation to calculate the distance, but the distance is essentially calculated as the difference between the two time series at each time point and summed over all time points. The greater this value the further apart the two time series are over the time period so this can be used to give a measure of how similar the two time series are.

There are other distance measures, which account for the temporal aspect and are therefore more appropriate to compare time series. The first order temporal correlation coefficient is one of these, giving a result between -1 and 1, where 1 indicates that both time series behave in a very similar way in both their direction and rate, -1 indicates that the rate of change is similar but that they move in opposite directions and 0 indicates that there is no similarity in the behaviour between the two time series. There are packages available in R, including TSclust, which can be used to determine the various distance measures available.

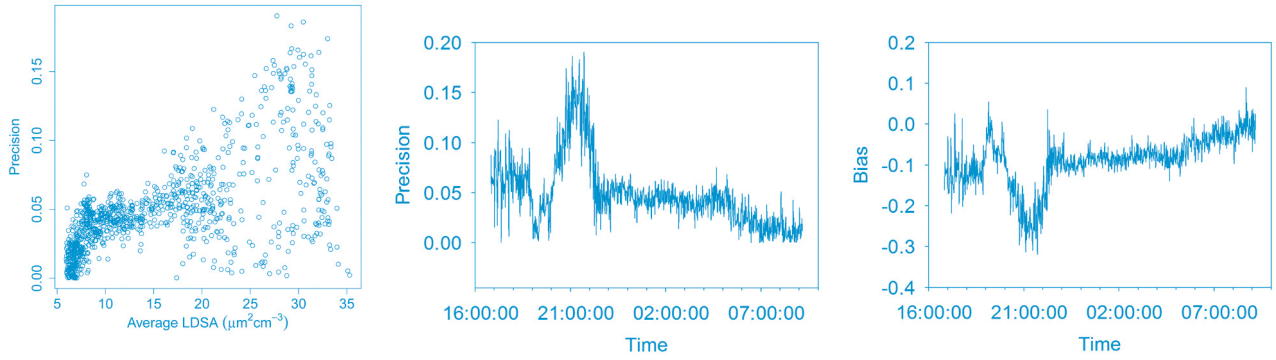


FIGURE 17: Precision and Bias by concentration and time.

4.2.2.4. Auto-Regressive Integrated Moving Average (ARIMA) models

The final method utilised in nanoIndEx is ARIMA models. These models are designed to specifically analyse time series data. The model is split into three main components: Auto-Regressive (AR), which takes current values to be a linear combination of previous values, plus white noise; Moving Average (MA), which consider linear combinations of the white noise inputs. These can be combined in an ARMA model, which when extended to also include considerations of non-stationarity of the time series result in ARIMA models. ARIMA models, can be fitted using a variety of statistical software, in R the forecast package is one package that allows for the fitting of ARIMA models. These can be fitted using the arima function and experimenting with the choices for AR, I and MA. The optimal values of these functions are chosen by examining plots of auto-correlation and partial auto-correlation of the residuals as well as comparing between models using the AIC. Within this package there is also an option to fit the best fit ARIMA model to the data, using auto.arima. The resulting model allows for the average concentration over the time period to be calculated, while taking account of the correlations between points in the time series. Using the functions available in R, and other packages, it is possible to compare different periods within a single time series (i.e. comparing between background and tasks where the measurements are taken sequentially).

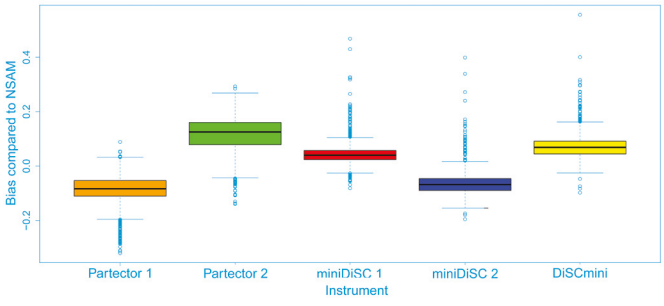


FIGURE 18: Boxplot of precision of different instruments.

Chapter 5

Exemplary data from field measurements

5.1. Experimental

Field measurements conducted in the scope of the project nanoIndEx used stationary and personal instruments and have underlined the importance of personal instrumentation for individual exposure measurement. Personal monitors used included the partector, partector TEM, DiSCmini, nanoTracer and in a single case the PUFP C100. PGP and NANOBADGE were used as commercial personal samplers in addition to a few prototypes. Samples for electron microscopic analyses were taken with Partector TEM and ESPnano. Stationary measurement equipment comprised the state of the art aerosol instrumentation, including scanning mobility particle sizers (SMPS), fast mobility particle sizers (FMPS), condensation particle counters (CPC), optical particle counters (OPC), aerodynamic particle sizers (APS), and electrostatic precipitator samplers for collecting particles for subsequent analyses. The suite of instruments for a measurement campaign was chosen based on the materials and activities in the workplace.

During the performed measurements, the results of personal instruments were compared to those of stationary instruments, which were placed in the near and far field of the emission source or in the background. Movements of workers carrying personal instrumentation through the room were protocoled to test for correlations between personal and stationary instruments at selected situations and locations.

5.2. Field study during preparation of pastes

Field measurements were performed in an industrial pilot plant during preparation of polymer-based conductive impregnation pastes from nanostructured exfoliated graphites. The worker was wearing full personal protection and moving freely between the mixer station and the nearby powder store. The work was interrupted from time to time for removal of powder spills by vacuum cleaning. No local exhaust ventilation was installed at the mixer. A comparison of personal and stationary monitor responses in the near field at the mixer and the far field in the pilot plant hall is shown in Figure 19. While the far field particle number concentration was hardly increased during the mixing task, the individual dose frequently exceeded peak concentrations of 100 000 cm^{-3} and was 5 times higher than in the far field on average. The near field monitor was placed directly next to the mixer. However, since the room ventilation was unintentionally directed from the near field monitor inlet towards the emission source, the near field device detected only few peaks and three times lower average concentrations.

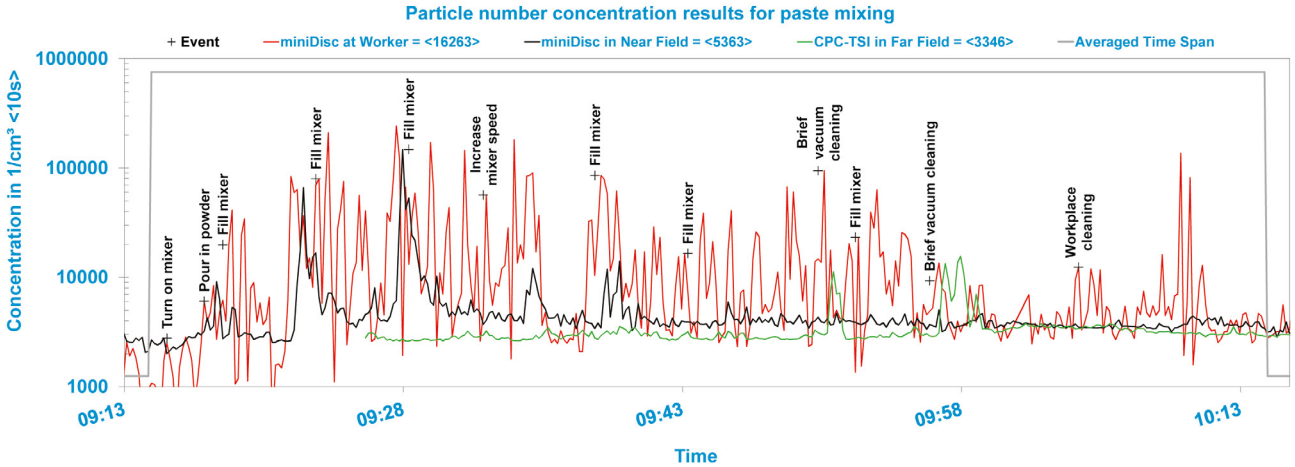


FIGURE 19: Comparison of worker, near and far field particle number concentrations during preparation of a MNM-containing paste involving dry powder handling and mixing. The numbers given in angle brackets in the legend are mean values obtained by averaging the data over the time span indicated by the grey frame.

This shows that only personal instrumentation in the breathing zone is capable of measuring MNM exposure, whereas stationary instruments can only measure emission. This way, personal monitors were shown to be capable of identifying unknown emission sources and peak emissions related to specific work tasks. Different to stationary devices they are not affected by unknown room ventilation conditions. Room airflow not directed from emission source to a stationary instrument dilute peak emissions into larger room volumes before being detected by the stationary monitor. This makes an identification of critical work tasks that cause strong peak emissions complicated or impossible. From an occupational hygiene point of view it is desirable to reduce the emission of critical work tasks, to test and optimise the effectiveness of local ventilation measures and to implement more adequate preventive and protective measures.

5.3. Field study during production of TiO_2 nanoparticles

Another field study was conducted in a pilot plant for the production of iron doped TiO_2 nanoparticles. A fast mobility particle sizer (FMPS) was used to monitor the far field. The lung deposited surface area concentration in the far field was calculated from the measured size distributions by assuming particles to be spherical. Several workers in the facility were equipped with personal monitors and personal samplers. Figure 20 shows an example for a time series plot of the LDSA concentration measured in the far field with the FMPS and the personal exposure of a worker in terms of LDSA concentration, measured with a partector. The time series can be split into three phases. Initially, the worker conducted regular work inside the facility, where no local emission source was detected. Later, during the lunch break, the partector was placed near the FMPS to recharge and for a side by side comparison of the instruments. Finally after the lunch break, the worker continued with his activities, but a strong local emission of NaCl particles was deliberately initiated inside the production facility. Figure 20 clearly shows that during periods with no local emission, the concentrations measured in the far field and on the person agreed rather well. The same is true during the side by side comparison, whereas with the strong local source, the personal exposure concentration was much higher than the far field concentration.

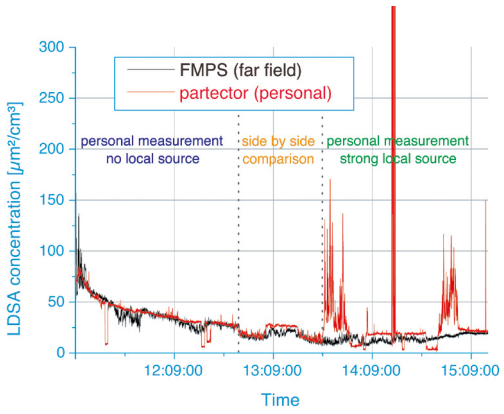


FIGURE 20: Time series plot of the lung deposited surface area concentration measured in the far field with FMPS and personal exposure measured with a partector.

A scatter plot of the same data as in Figure 20 is given in Figure 21. The plot also represents the rather good agreement of the data measured side by side and with no local source. The negative spikes in the scatter plot during the measurements without local source (blue) stem from short periods, where the worker entered a room with filtered air supply. These are also clearly visible in Figure 20 at 11:27, 12:25 and 12:30.

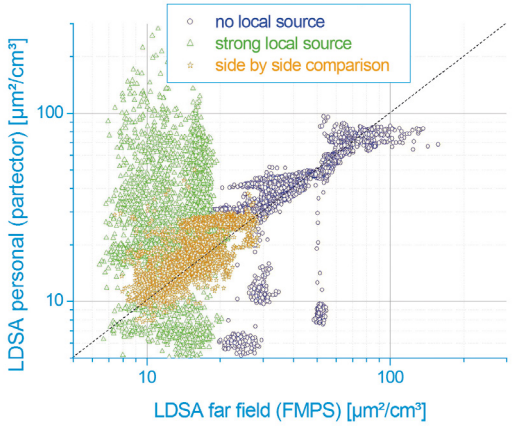


FIGURE 21: Scatter plot of the LDSA concentration measured in the far field with an FMPS and personal exposure concentration measured with a partector; different colours refer to the three phases, specified in Figure 20.

Figure 22 shows an example of XRF analysis on the four main elements measured on the NANOBADGE filters (Ti, Fe, Ca and Cl). Two samplers were worn by a worker (positioned on left and right chest in the breathing zone) over the whole shift while two others were respectively located at the source (near field) and in the main hall for background measurement (far field).

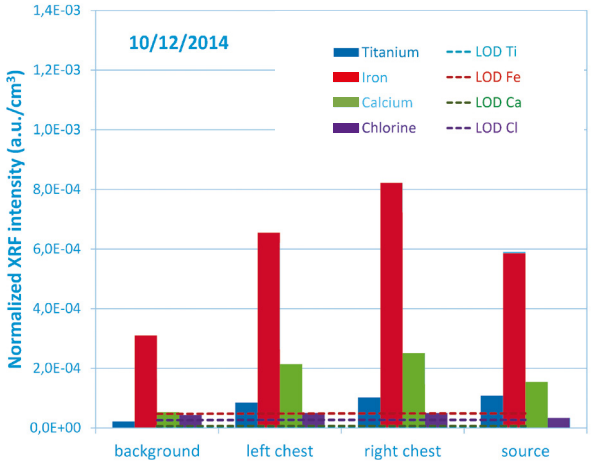


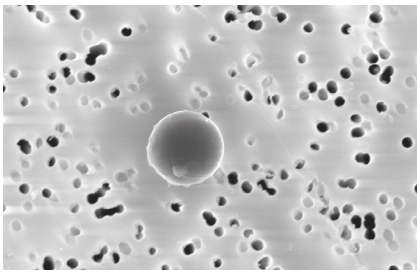
FIGURE 22: XRF analysis of the NANOBADGE filters from one day of measurement.

During that day, the TiO_2 pyrolysis reactor was emptied and cleaned. It has been shown based on XRF analysis that the quantity of titanum on the "source" filter was 7 times higher on that day than on the day before when the reactor was kept closed. Figure 25 shows SEM images of the highly agglomerated nanoparticles of TiO_2 emitted during the cleaning step at the "source".

The calculated mass concentration of TiO_2 measured with the two NANOBADGE respectively for left and right chest was 1.31 and 1.57 µg/m³ averaged over the whole shift. SEM images confirm the presence of nanostructured particles of TiO_2 on the filters as shown in Figure 24. Those values remains much lower than the REL of the NIOSH [27] (300 µg/m³). Iron originating certainly from machining and welding activities in the surrounding area has also been detected and confirmed by SEM images (Figure 23).

5.4. Field study in a laboratory for the synthesis of nanowires

A field study was conducted in a nanotechnology research facility, where among others nanowires are produced. The laboratory has a filtered air supply. Background particle concentrations in the room were therefore quite low. This study was conducted according to tier 2 of a tiered approach, i.e. solely with portable and personal measurement equipment. The instrumentation used included DiSCmini,



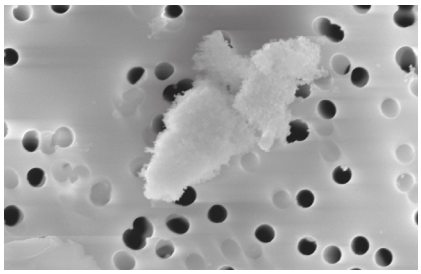
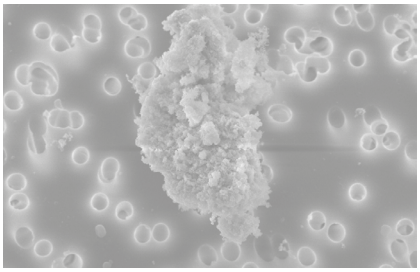
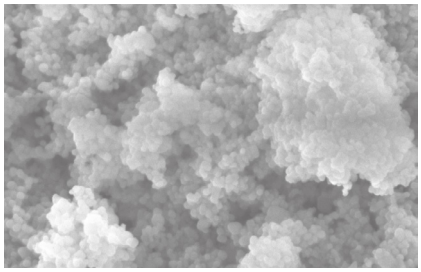


FIGURE 23: SEM images from the NANOBADGE filers showing Fe-based spherical particles.

FIGURE 24: SEM images from the NANOBADGE filers showing nanostructured TiO_2 particles.





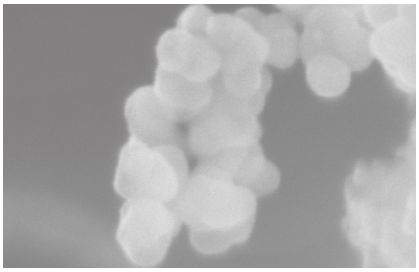


FIGURE 25: SEM images from the NANOBADGE filers (source) showing highly agglomerated TiO_2 nanoparticles.

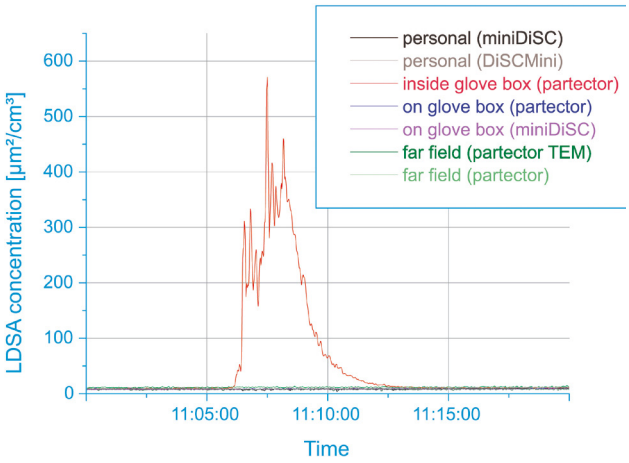


FIGURE 26: Time series of lung deposited surface area concentration measurement in a tier 2 assessment of the exposure in a research facility during the preparation of a substrate for the synthesis of nanowires.

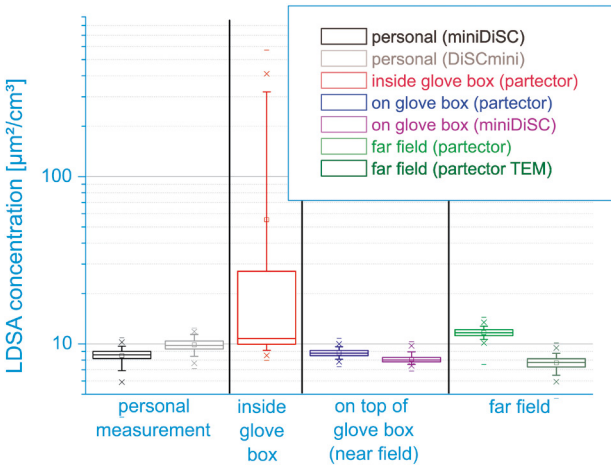


FIGURE 27: Box plots of the data measured in a tier 2 assessment of the exposure during preparation for the synthesis of nanowires.

partector, partector TEM, PUFP C100, ESPnano as well as prototypes of personal samplers. During this measurement campaign, several monitors were placed in different far field locations to keep track of potential spatial concentration differences. At least one of the local staff and one of the nanoIndEx investigators carried a personal exposure monitor.

Figure 26 presents the time series of the lung deposited surface area concentration during a single task, i.e. preparation of a substrate for the synthesis of nanowires. This included the transfer of a wafer chunk into a glove box, in which Indium was melted on a hot plate to treat the wafer. The personal exposure of two people inside the laboratory was monitored with one miniDiSC/DiSCmini each. One partector was located inside the glove box and another partector on top of the glove box such that it would aspire particle potentially released through the openings for the gloves. Another miniDiSC was collocated to the partector. The glove box was maintained at under pressure, a release from the glove box under normal operation would thus be quite unlikely. One partector and one partector TEM were additionally placed several meters away from the glove box to monitor the far field concentration. Figure 26 shows that all instruments measuring outside the glove box showed very low and constant concentrations, whereas the partector inside the glove box measured significantly higher concentrations during the period from 11:05 to 11:13, when the hot plate was switched on. The same data as shown in Figure 26 are presented as box plots in Figure 27. The graphs clearly show that only the concentration inside the glove box increased to high levels, whereas all the other concentrations, including the personal exposure concentrations remained quite low and comparable with each other. Only one partector in the far field consistently measured higher concentrations than the others, which, however, do not seem to be correlated with any activities in the laboratory. The reason for the slightly higher concentration measured with this instrument remains unclear.

Nevertheless, the tier 2 assessment proved that the safety measures in place, i.e. e. operating in a glove box, are effective and efficiently prevent the operators from exposure to nanomaterials.

5.5. Conclusions from field studies

The use of personal samplers and monitors to evaluate individual occupational exposure of workers to MNMs can significantly improve the process of risk assessment and risk management. In fact, personal monitoring and sampling has proven capable of providing relevant and reliable data regarding the individual exposure of workers. In some cases the personal equipment has proven to be superior over static devices, in cases with high spatial variability of the workplace aerosol.

Chapter 6

Lessons learned during the project

As Thorstein Veblen pointed out, serious research will always generate new open questions, and a good research project will teach the researchers several lessons. During the nanoIndEx project, many new questions came up. Some of them were rather easy to answer, while it took us quite some effort to tackle others and to learn our lessons. And of course some questions still remain open to make our future interesting. In this chapter, we would like to share with you the roads we have travelled during the nanoIndEx project, so that you can take a shortcut without duplicating our detours.

6.1. Lesson 1: Instrumental issues

By comparing the sheer size of a personal monitor with the size of conventional aerosol measurement equipment, it becomes obvious that something has to be compromised. While the partector is just a little larger than the size of a cigarette box, an FMPS weighs 32 kg and has half the size of a dishwasher. In order to be so small, most personal monitors use the indirect measurement principle of charging the incoming particles and measure a current, induced by the so-charged particles. The interpretation of this current is based on several assumptions and only holds in a certain size range. We provided experimental proof for the prior assumption that these instruments are only able of determining the number and LDSA concentration for particles between 20 nm and 400 nm. The expected accuracy and comparability of LDSA concentration measurements is in the range of ±30%. For number concentration measurements with diffusion chargers it is lower. While the accuracy and comparability of the personal monitors are hence certainly below those of conventional aerosol measurement equipment, the instruments still provide reasonably good and sufficiently accurate data on the personal exposure.

The only available personal (water based) condensation particle counter PUFP C100 was only shortly available within nanoIndEx. The comparability of number concentrations measured with the PUFP C100 with those measured with stationary CPCs was typically ± 10 % or better. The instrument also covers a broader size range than the diffusion chargers, i.e. from 4.5 nm up to several micrometers. However, when the particles are highly hydrophobic (pure DEHS), the PUFP C100 reported back drastically too low concentrations. To the contrary, the agreement was much better, when the DEHS contained only minor impurities. Also measurements with hydrophobic soot-like carbon particles delivered very good and accurate results. It can therefore be expected that the PUFP C100 is able to measure the number concentration in almost any real workplace setting, where highly pure hydrophobic substances are rather unlikely.

Another issue we noticed related to the instruments is that the internal clocks were rather inaccurate. Proper synchronisation of the instrument clocks is, however, inevitable. With the available instruments, at least daily synchronisation is required. Manufacturers are encouraged to use better clocks that synchronise themselves, based on a radio signal, or automatically synchronise with a computer clock as soon as the device is connected.

6.2. Lesson 2: Issues related to planning and performance of field measurements

We had to learn the hard way that positioning of the static instruments for near field, far field and/or background measurements needs to take into considerations many factors. Any air flows and especially their 3 dimensional direction need to be determined, as otherwise, for example the near field monitors may not be affected by the activity, whereas in extreme cases, even the background or far field can be biased.

Another important topic that needs to be discussed and concluded beforehand is whether

short and task based exposures/doses are to be determined or if shift based averages are required. If the latter is needed, the highly time resolved dataset of personal monitors can be drastically reduced to be handled more easily (see below).

6.3. Lesson 3: Issues related to personal monitoring

An important question in personal exposure measurements is always where in the breathing zone to fix the sampling inlet. The aspiration efficiency can be affected by many parameters, including the activity and whether the person is left- or right handed. In a dedicated laboratory study, we exposed two individuals to NaCl aerosol, while they were carrying out certain activities. Both carried two identical personal monitors both sampling from the breathing zone, one from near the left and the other from near the right collar bone. No significant differences were found (see Figure 14) for measurements carried out with partector without sampling tubes. We therefore conclude that the placement of the sampling inlet (left vs. right) is not critical.

The other individual in the chamber was equipped with miniDiSC instruments, which sampled through 75 cm long conductive silicone tubes. These tubes are typically considered as the optimum for transporting aerosols through flexible tubes, because they minimise particle losses. Both person carried miniDiSC drastically underreported the airborne particle concentrations. The results were the probably biggest surprise we experienced during the project and can have a major impact on personal exposure monitoring with diffusion chargers. When we investigated the reasons for the discrepancy further, we noticed that degassing of siloxanes from the silicone tubing affected the ion properties in the charger of the miniDiSC, resulting in too low currents to be measured. The currents are then misinterpreted as low particle concentrations. This effect was particularly pronounced in case of DiSCmini, but still noticeable with partector.

We conducted a thorough study on the effect of different types of tubing on the measurement and concluded that currently Tygon® seems to be the most recommendable tube material.

6.4. Lesson 4: Issues related to personal sampling

One critical point in personal particle sampling for subsequent analyses is that the samplers typically operate at rather low flow rates, among others to keep pump requirements low. On the other side, the analytical techniques used to evaluate the samples need a certain minimum amount of material to be analysed (LOD). Especially in case of samples for electron microscopic analyses, it can be quite difficult to determine the correct sampling time. The challenge is to collect enough material to provide proper statistics, but at the same time not to overload the sample. Partector TEM suggests a sampling time for optimal coverage of the substrate. However, in several cases, we found the duration of a task to be monitored to be much too short for the suggested time, especially if the particle concentrations are low.

Besides commercial personal samplers, we also used a few prototype samplers in nanoIndEx. Two of them use an impaction stage with a cut off size at only 100 nm. Such an impactor generates a high pressure drop, which requires a strong pump and reduces the battery lifetime of the pump. We found that with the tested samplers, 8 hour operation of the personal pumps was impossible as the batteries were typically empty after 4–6 hours already.

6.5. Lesson 5: Data collection and handling

Collection and handling of personal exposure measurements with highly time resolved monitors can be quite challenging. Monitors with 1 s time resolution produce 3600 data points per hour or 28,800 data points per 8 h shift. If several monitors are used, like in the examples

in chapter 5, one may not only easily loose overview of the data. The spreadsheet files get quite large, especially when plotting the data with 1 s time resolution, which many times caused software or computer crash. It is hence very recommendable to prepare clear spreadsheets and to reduce the amount of data through averaging where possible. If data reduction is not possible, the number of diagrams per file should be limited.

It is inevitable to take many notes during field measurements. We also found it useful to have more than a single person taking notes. Although meanwhile we take the utmost care to record every even minor incident during the measurements, we eventually typically still find that something is missing in our records. A possibility for event logging in the monitors would therefore be very welcome. Currently, only the NanoTracer offers the possibility to flag the dataset at user definable time spots.

Besides the measurement data, a lot of contextual information concerning the worker, workplace, materials, etc. is needed. The amount of data that can be put into the NECID database seems infinite and initially we were a bit stumped. In order to provide a better overview of what is really needed, nanoIndEx developed data collection and data input protocols that make life a lot easier now.

6.6. Lesson 6: Sampling or monitoring? What metric should be determined?

There are no clear and simple answers to these questions. Of course, if exposure during short tasks shall be determined, only monitors with high time resolution can be used. Samplers might be used for 15 min sampling as long as the analytical techniques used to characterise and quantify the collected material have a sufficiently low limit of detection. If the goal is to produce shift averages, the use of samplers is also feasible. Another main question is the metric to be determined. Currently, the number and LDSA concentration can only be determined with monitors (exception: sampling and electron microscopic analysis, but this is very time consuming), whereas the mass concentration can only be determined with reasonable accuracy by using filter samples. If exposure to a specific chemical entity shall be determined, this can currently only be achieved by sampling and subsequent chemical analysis.

While monitors provide more (time resolved) information, this also means that more information needs to be analysed, whereas the analysis of samplers directly provides a single value which can be more easily used in worker medical files or future epidemiological studies.

Workplaces measurements generally present particle spectra of unknown composition. Individual MNM exposure assessment at workplaces thus often requires a combination of monitoring and sampling instruments. Any exposure causes a particle type- and size-dependent dose. For a better distinction, not only particle number or mass concentrations are to be determined but the MNM dose must be differentiated by identity and origin. This requires morphological and chemical composition analysis of sampled particles by microscopy and X-ray (XRF, EDX) or Raman spectroscopy. This way information can be generated that is necessary to distinguish manufactured nanoparticle from those originating from natural or background sources like combustion and road traffic.

Chapter 7

Conclusions

When we started nanoIndEx in June 2013, not much was known about the possibilities, the novel personal monitors and samplers offer and how they can be utilised in exposure assessment. In the project we looked into the most pressing questions, like the accuracy and comparability of the samplers and monitors, their field applicability, how field measurements can be conducted and what kind of data needs to be collected. Those pressing questions are now answered. The personal instruments studied in the project nanoIndEx will contribute to progress in the field of nanotoxicology since they are capable of characterising personal exposure levels in terms of different dose-metrics. In fact, one of the main issues in the context of MNM-related risk assessment is hazard characterisation. It is primarily based on in vitro and in vivo toxicological studies to investigate MNM-specific toxicity and to clarify relationships between the physical and chemical properties of MNMs and their induction of toxic biological responses. Unfortunately, many nanotoxicological studies have used excessive, unrealistically high doses of MNMs and it is therefore debatable what their findings mean for the lower real-world exposures of humans. Moreover, it is not clear how to establish realistic exposure dose testing in toxicological studies, as available data on occupational exposure levels are still sparse. Future toxicological studies should focus on potentially adverse effects of low-level and realistic MNMs exposure, especially through the use of exposure doses similar to those identified in environmental sampling. The use of personal instruments like the ones evaluated in nanoIndEx will facilitate the determination of realistic (low) exposure and dose levels expressed in different dose-metrics. They will thus provide extremely useful information to nanotoxicologists and help to implement well-designed in vitro and in vivo studies based on realistic exposure doses.

nanoIndEx has thus laid the foundation for future assessment of personal exposure to airborne nanomaterials, facilitating epidemiological and more meaningful toxicological studies.

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