The Handbook of Environmental Chemistry 48

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Mar Viana *Editor*

Indoor and Outdoor Nanoparticles

Determinants of Release and Exposure Scenarios

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The Handbook of Environmental Chemistry

Founded by Otto Hutzinger

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Volume 48

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Indoor and Outdoor Nanoparticles

Determinants of Release and Exposure Scenarios

Volume Editor: Mar Viana

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Aims and Scope

Since 1980, *The Handbook of Environmental Chemistry* has provided sound and solid knowledge about environmental topics from a chemical perspective. Presenting a wide spectrum of viewpoints and approaches, the series now covers topics such as local and global changes of natural environment and climate; anthropogenic impact on the environment; water, air and soil pollution; remediation and waste characterization; environmental contaminants; biogeochemistry; geoecology; chemical reactions and processes; chemical and biological transformations as well as physical transport of chemicals in the environment; or environmental modeling. A particular focus of the series lies on methodological advances in environmental analytical chemistry.

Series Preface

With remarkable vision, Prof. Otto Hutzinger initiated *The Handbook of Environmental Chemistry* in 1980 and became the founding Editor-in-Chief. At that time, environmental chemistry was an emerging field, aiming at a complete description of the Earth's environment, encompassing the physical, chemical, biological, and geological transformations of chemical substances occurring on a local as well as a global scale. Environmental chemistry was intended to provide an account of the impact of man's activities on the natural environment by describing observed changes.

While a considerable amount of knowledge has been accumulated over the last three decades, as reflected in the more than 70 volumes of *The Handbook of Environmental Chemistry,* there are still many scientific and policy challenges ahead due to the complexity and interdisciplinary nature of the field. The series will therefore continue to provide compilations of current knowledge. Contributions are written by leading experts with practical experience in their fields. *The Handbook of Environmental Chemistry* grows with the increases in our scientific understanding, and provides a valuable source not only for scientists but also for environmental managers and decision-makers. Today, the series covers a broad range of environmental topics from a chemical perspective, including methodological advances in environmental analytical chemistry.

In recent years, there has been a growing tendency to include subject matter of societal relevance in the broad view of environmental chemistry. Topics include life cycle analysis, environmental management, sustainable development, and socio-economic, legal and even political problems, among others. While these topics are of great importance for the development and acceptance of *The Handbook of Environmental Chemistry,* the publisher and Editors-in-Chief have decided to keep the handbook essentially a source of information on "hard sciences" with a particular emphasis on chemistry, but also covering biology, geology, hydrology and engineering as applied to environmental sciences.

The volumes of the series are written at an advanced level, addressing the needs of both researchers and graduate students, as well as of people outside the field of "pure" chemistry, including those in industry, business, government, research establishments, and public interest groups. It would be very satisfying to see these volumes used as a basis for graduate courses in environmental chemistry. With its high standards of scientific quality and clarity, *The Handbook of Environmental Chemistry* provides a solid basis from which scientists can share their knowledge on the different aspects of environmental problems, presenting a wide spectrum of viewpoints and approaches.

The Handbook of Environmental Chemistry is available both in print and online via www.springerlink.com/content/110354/. Articles are published online as soon as they have been approved for publication. Authors, Volume Editors and Editors-in-Chief are rewarded by the broad acceptance of *The Handbook of Environmental Chemistry* by the scientific community, from whom suggestions for new topics to the Editors-in-Chief are always very welcome.

Damià Barceló
Andrey G. Kostianoy
Editors-in-Chief

Volume Preface

Nanotechnology is a strategic driver of innovation, which has been identified as a key enabling technology (KET) in Horizon 2020 to support industrial leadership in Europe. It involves the development and use of materials and objects at the nanoscale (1–100 nm). When intentionally manufactured, nanomaterials are frequently referred to as engineered nanomaterials (ENMs). However, nanoparticles (NPs) may also be unintentionally generated during industrial processes which do not involve nanomaterials as input or output products.

Due to the increasingly widespread use of nanomaterials, it is critical to identify any potential risks they may pose to human health or the environment. Nanosafety is concerned with the safe and sustainable development of nanotechnology, and it is a necessary tool to ensure the widespread application of nanotechnology without which the potential risks could overcome the expected benefits of nanotechnology applications. The need for effective risk governance, which is crucial when developing new technologies such as nanotechnologies, has been evidenced [1]. Furthermore, comprehensive roadmaps such as *Nanosafety in Europe 2015–2025* [2] provide a strategic vision for future research on the safe use and application of ENMs. Initiatives such as the Nanosafety Cluster initiative (http://www.nanosafetycluster.eu/) are succeeding in maximising the synergies between existing research projects addressing all aspects of nanosafety including toxicology, ecotoxicology, exposure assessment, mechanisms of interaction, risk assessment and standardisation.

In this framework, this volume aims to provide an overview of the determinants of release and exposure scenarios of airborne NPs, whether intentionally or unintentionally generated. The dosimetry and toxicology of nanosized particles and fibres are reviewed in the chapter "Dosimetry and Toxicology of Nano-Sized Particles & Fibres", highlighting their potential threat for human health and safety and discussing the main drivers of adverse health outcomes. The chapters "Measurement Methods for Nanoparticles in Indoor and Outdoor Air" and "Exposure Assessment: Methods" are devoted to NP measurement and exposure assessment methods and provide a comprehensive overview of the tools and strategies available to characterise exposures in indoor and outdoor settings. Special attention is given to knowledge gaps and to limitations with regard to current instrumentation and standardisation needs. NP sources, release mechanisms and determinants, including case studies, are discussed in the chapters "Occupational Release of Engineered Nanoparticles: A Review", "Nanoparticle Release in Indoor Workplaces: Emission Sources, Release Determinants, and Release Categories Based on Workplace Measurements", "Nanoparticles Release from Nano-Enabled Products" and "Workplace Exposure to Process-Generated Ultrafine and Nanoparticles in Ceramic Processes Using Laser Technology". These chapters review available studies which report on the release of airborne ENMs in different nanotechnology workplaces, covering topics of relevance to occupational exposure ranging from the identification of release mechanisms and scenarios to measurement methods and working towards a standardised approach to exposure characterisation. Use-phase release scenarios are also included, as well as protocols for product ageing and nanomaterial quantification and characterisation. Exposure assessments carried out in specific case studies involving ENMs (e.g. handling of bulk material at low energy, dispersion of highly concentrated NPs) and unintentionally generated NPs (e.g. during laser sintering of ceramic tiles) are described. Because experimental exposure studies must be complemented by modelling approaches, the chapter "Quantitative Modelling of Occupational Exposure to Airborne Nanoparticles" explores tools for quantitative modelling of occupational exposure to airborne nanoparticles, taking into account mechanisms determining the likelihood of release and transport of NPs in the workplace. Finally, the chapter "The Flows of Engineered Nanomaterials from Production, Use and Disposal to the Environment" evaluates what information is needed to quantify the flows of ENMs to the environment by reviewing the current state of knowledge, taking a life-cycle approach.

Nanotechnology is a rapidly evolving field, and as a result nanosafety research must also be in constant evolution. Because of its broad scope including NP measurements, modelling, toxicology, risk assessments and standardisation, among others, one single volume cannot aim to cover all the relevant aspects in this field. Examples of issues not addressed in this volume are emerging NP forms and applications, the need for enhanced instrumentation for online detection of ENMs in the workplace, or the need for a regulatory framework and standardisation guidelines, among others. Addressing these and other knowledge gaps will help to quantify the risks associated with nanomaterials and thus promote the safe, sustainable and responsible use of nanotechnology.

This book is intended for a broad audience, from specialists working already in the field to newcomers who want to gain insights into this topic. I would like to sincerely thank all the authors for their time and efforts in preparing their outstanding contributions to this volume, as well as my coworkers for creating a motivating work environment.

Barcelona, Spain Mar Viana

References

1. Read SA et al (2015) Foresight study on the risk governance of new technologies: the case of nanotechnology. Risk Anal. doi:10.1111/risa.12470
2. Savolainen et al (2013) Nanosafety in Europe 2015 – 2025: towards safe and sustainable nanomaterials and nanotechnology innovations. ISBN 978-952-261-310-3

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Dosimetry and Toxicology of Nanosized Particles and Fibres

Flemming R. Cassee, Wolfgang Kreyling, Rob Aitken, and Craig Poland

Abstract Once inhaled, nanomaterials (particles and fibres) have a high probability of deposition in the lungs mainly by diffusion and to be transported throughout the body. The chemical composition and surface reactivity and dissolution rates are the driving forces for toxicity often starting with oxidative stress which can lead to inflammation, systemic effects or even lung cancer.

Keywords Dosimetry, Inhalation, Nanomaterials (particles and fibres), Translocation toxicity

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1 Introduction

Once inhaled, nanoparticles (NPs) have a high probability of deposition in the lungs. This deposition occurs primarily by diffusion and secondarily by thermophoretic effects in the first few airways of the lung during inhalation. NP between 20 and 100 nm will deposit predominantly in the alveoli and small airways. Fibres and platelets like graphene that are nanosized in at least one dimension are also deposited in the lower respiratory tract, mainly by interception due to their small size and elongated shape. Once deposited the chemical composition and surface reactivity and dissolution rates are the driving forces for toxicity. Often, the toxicity is driven by oxidative stress leading to inflammatory responses and tissue damage as well as lung cancer including mesothelioma related to persistent fibres. Particles can be translocated across the blood–air barrier into blood circulation and accumulate in other organs where they can also cause and/or trigger to adverse health outcomes.

2 Factors That Affect Deposition and Clearance

Inhalation of airborne particles including nanoparticles (NP; $<$ 100 nm) will lead to their deposition onto the regional epithelia of the respiratory tract depending on (1) the aerodynamic and thermodynamic properties of the particles and, only for NP, (2) the geometric branching pattern of the airways and alveoli and (3) the breathing pattern of the human subject [1–4]. Whilst impaction and interception are factors that are more dominant for micro-sized particles, nanosized particle depositions are more driven by diffusion (in particular at low air speed) and surface charge (Fig. 1).

Once deposited, the particles will interact first with the surfactant film and epithelial lining fluid and subsequently with cells of the epithelium. An important consideration in the deposition of particles into the lung-lining fluid is the rich composition of surfactant film (a complex mixture of lipids and surfactant proteins) and the fact that any depositing material quickly becomes coated in these surfactant proteins and lipids. The benefits of such a coating for innate immunity are obvious, as key proteins such as surfactant protein (SP)-A and SP-D bind a variety of pathogens [5], but such a coating also gives the deposited particle its 'biological identity' [6, 7] – it's so-called protein corona. As such, a coating is not specific to nanoparticles, and indeed particles (any depositing matter such as bacteria would also become coated) are subject to modification and can be completely removed by uptake by a cellular phagolysosome [8], its specific impact on the toxicological

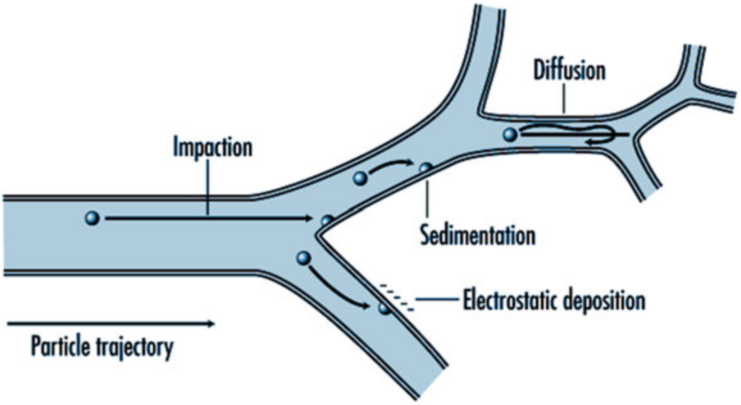

Fig. 1 The mechanisms accounting the deposition of inhaled particles in the respiratory system during the inspiration: impaction/interception, gravimetric sedimentation and diffusion are the main drivers followed by electrostatic deposition

profile of a nanomaterial has yet to be fully elucidated but it is likely to play a role in the way particles interact with lung cells such as alveolar macrophages [7].

All of these processes are part of the lungs' multiple defence mechanisms but are also essential for the physiological functioning of the lung and keeping the gas exchange region clear. Whilst macrophages provide a major line of defence for micron-sized particles, the other mechanisms play a pivotal role for NP blood distribution (Fig. 2).

Particle clearance out of the respiratory tract comprises different elimination processes including mechanisms of particle transport and mechanisms of particle digestion/dissolution. Particle translocation as a subset of clearance mechanisms refers to the migration of particles from their primary portal of entry (organ of deposition; here the respiratory tract) into other (secondary) organs. The process of translocation implies that the NPs penetrate at least one body membrane. Among other parameters the translocation rate and fraction depend on particle size and morphology and surface parameters such as composition and charge. Since the translocation rate becomes negligible for particles larger than about 300–500 nm – except in particle overload conditions and severe inflammatory states – detailed experimental evidence for translocation exists only for NP in rodents; unfortunately almost no human NP translocation data exist. After deposition on the alveolar epithelium, NPs have to cross the blood–air barrier, in order to enter the circulation. Factors affecting biokinetics of inhaled NP in the lungs are schematically outlined in Fig. 3 as part of the exposure–dose–response paradigm.

3 Deposition Patterns of Spherical Nanoparticles in the Human Respiratory Tract

The dependence of total deposition in the human respiratory tract, consisting of extrathoracic (head), tracheobronchial (TB) and pulmonary (PUL) region, is plotted in Fig. 4 for particle diameters ranging from 1 nm to 10 μm for oral and nasal

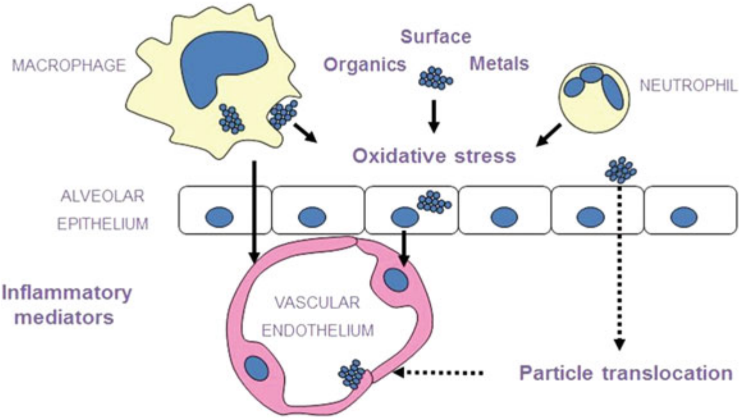

Fig. 2 Schematic presentation of the interaction of particles with the biological (defence) system and translocation mechanism in the lung. Particles can interact with or can be phagocytized by free-moving macrophages or can directly interact with the epithelial cells. Cells can response by releasing mediators attracting inflammatory cells (neutrophils). Particles can also pass through cells or in between cells reaching the blood vessels and blood

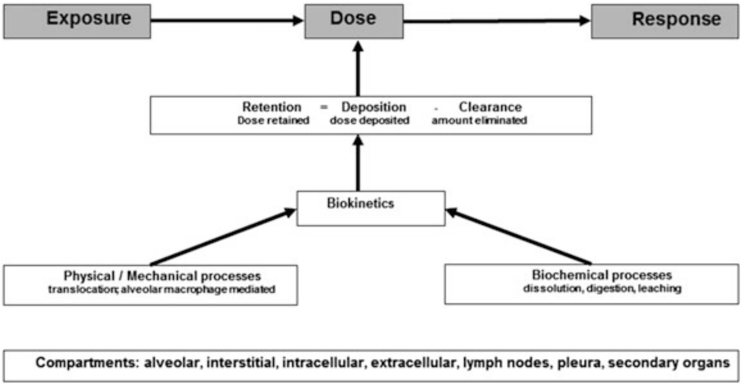

Fig. 3 Biokinetics associated with the exposure–dose–response paradigm (Adapted from [9])

inhalation by a 21-year-old male adult under breathing conditions sitting at rest, using the MPPD V2.1 model.[1] This figure illustrates the relatively high deposition of nanoparticles, compared to submicrometer-sized particles, which may contribute to the significant risk for detrimental health effects. Deposition of nanoparticles with diameters between 1 and 100 nm increases with decreasing particle size, consistent with diffusional deposition by Brownian motion. In contrast to large

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[1] http://www.ara.com/products/mppd.htm

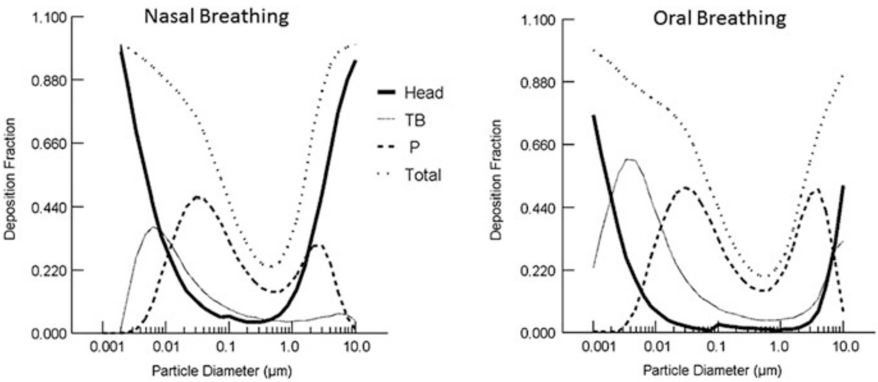

Fig. 4 Impact of nasal versus oral breathing on particle deposition in the respiratory tract and lungs of an adult (MPPD v2.1)

particles, the route of inhalation, either via nose or via mouth, hardly affects the total deposition.

Regional deposition in the TB and PUL regions via oral and nasal inhalation is shown in Fig. 4, for breathing conditions sitting at rest using the MPPD model [10]. Since PUL volumes were identical among all lung geometries, deposition calculations in these limiting geometries provided the bound for the predictions. The figures exhibit similar deposition patterns for different particle sizes. However, because of more efficient removal of nanoparticles in the nasal region, less particle penetration and deposition occur with nasal breathing. In fact, 2-nm and smaller size particle deposition is 100% in the nasal airways, and subsequently there is no TB and PUL depositions. In addition, the calculated total deposited fraction gives a narrow variation in deposition for different size particles and is almost independent of airway geometries. Thus, detailed configuration of the conducting airways has a minor influence on total deposition as long as lung volumes are the same. This is particularly true for particles smaller than 3 nm and larger than 40 nm. The variation in TB deposition is also insignificant for particles smaller than 3 nm and remains below 20% for larger size particles. The largest influence of lung geometry on deposition occurs in the PUL region. Despite the fact that all geometries use the same alveolar structure, a noticeable variation in PUL deposition is observed with using different lung geometries. This behaviour may be explained in terms of the filtering effects of the ET and TB regions. Higher and lower heads and TB depositions yield lower and higher PUL depositions, respectively. As a result, total deposition seems to be insensitive to the structure of lung geometry. In addition, pulmonary deposition occurs only in those alveolar regions which are ventilated, i.e. there is very limited diffusion of NP into areas of residual gas volumes as well as of non-ventilated diseased peripheral lungs.

Total deposition of nanoparticles in the human lung, i.e. in the TB and PUL regions, for different breathing patterns is shown in Fig. 5 for nanoparticles ranging in size from 1 to 100 nm under nasal and oral inhalation conditions. The theory of diffusional deposition by Brownian motion predicts that the lower the flow rate at a fixed inhaled volume, the higher is the residence time and hence the probability of deposition by diffusion. However, the opposite trend can be observed in this figure, i.e. deposition decreases for higher flow rates at a fixed inhaled volume. This unexpected behaviour can be explained by the filtering efficiency of the nose, since slower breathing increases deposition in the nasal passages upon inspiration. This reduces the number of particles entering the trachea and leads to smaller deposition fractions in the lungs despite their higher deposition probability in the bronchial and alveolar airways. The downturn of the deposition fraction in the range from 10 to 1 nm is also caused by the increasing filtering efficiency of the nose with diminishing particle diameter. For the comparison of different respiratory conditions, it is important to note that the deposition fractions exhibited in Fig. 5 refer to the fractions of particles deposited in a single breath. However, a higher physical activity also leads to a larger number of particles inhaled per unit time, say in a minute, thereby further enhancing the differences.

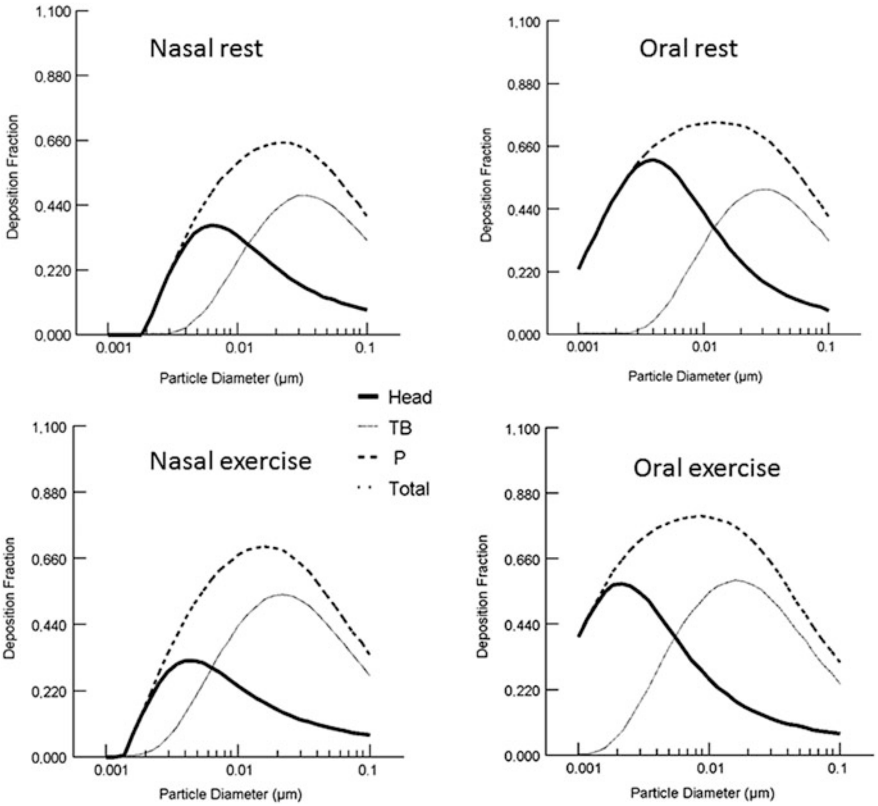

Fig. 5 Impact of rest versus exercise on nanoparticle deposition in the lungs of an adult (MPPD v2.1)

4 Deposition Patterns of Fibres in the Human Respiratory Tract

When considering the inhalation and deposition of fibres in the lung, it is useful to reflect that a *respirable* fibre is defined by the World Health Organization (WHO) in their guidelines for determining airborne fibre number concentrations [11] as having a length greater than 5 μm, a diameter a less than 3 μm and a length to width ratio (its aspect ratio) of greater than 3:1.

However, given that the particle size having 50% penetration for the non-ciliated, respirable zone fractions is 4.0 μm [12], it seems unlikely that a particle of >5 μm could be respirable let alone a fibre reaching upwards of 50 μm, yet such fibres do reach the alveolar region of the lung due to a peculiarity of fibre aerodynamics. In order to be inhaled, a fibre must still possess a single aspect (diameter) of less than 3 μm (hence, the WHO definition of possessing a diameter of <3 μm) but can have a length many times this. This is because the aerodynamic diameter is proportional to the fibre diameter, possibly due to the fibre reaching a preferred orientation by aligning itself axially due to airflow across the fibre surface [13, 14]. This results in a small aerodynamic diameter which only very slightly with increasing aspect ratio [15].

Whilst a long fibre may possess the same aerodynamic diameter as a small particle and hence be subject to similar routes of deposition (e.g. sedimentation, impaction, etc.), its length would increase the potential for deposition due to interception [16], although this typically happens in the larger airways where airflow is more rapid and able to propel the fibres out of a deviating airstream [14, 16]. Indeed mathematical modelling of fibre deposition in bronchial airways showed that deposition increased with fibre length as well as rising flow rates and branching angle of the airways and that hot spots of deposition occur at the cranial ridges [14].

What is understood about the deposition of fibres in the lung primarily comes from studies and simulations considering larger fibres such as asbestos and man-made vitreous fibres; however, it is difficult to know how this may relate to the deposition of fibrous nanoparticles in the respiratory tract. If we apply the definition of a fibre detailed above to nanofibres, this means that with a very narrow diameter (<100 nm as per the nano-definition), they should also display a length greater than 5 μm. This long length may, as with conventional fibres, result in increased deposition due to interception, yet the low diameter and overall mass of the fibre could mean that levels of impaction and interception due to high flow rates propelling the fibres out of a bending airstream in the upper airways are reduced. However, there is a paucity of experimental evidence to confirm or refute such a hypothesis.

One notable publication on the deposition of fibres in the lung that has considered particles in the nano-range is that of Sturm and Hofmann [16]. Within their calculations of fibre deposition for an array of fibre sizes, they considered fibres with cylindrical diameters ranging from 10 μm down to 1 nm across aspect ratios from 3 to 100. They found that fibre aerodynamic diameter was rather insensitive to aspect ratio in the case of nanoparticles even though it was of increased importance for larger particles (i.e. >100 nm). Interestingly the results led the authors to conclude that fibres with a diameter <200 nm exhibit a negative correlation with the aspect ratio; specifically, as we move into the nano-range, increasing fibre length causes a reduction of particle deposition by Brownian diffusion, finally resulting in a slight enhancement of the exhaled particle fraction [16]. For larger diameter fibres (>200 nm), there is a well-described positive correlation between aspect ratio and deposition by impaction, interception and sedimentation.

Another consideration is also shape, as when we consider fibre dimension and shape, it is the amphibole type fibres that come to mind, yet whilst this is reflective of amphibole asbestos and MMVF, it does not reflect more curved structures as seen with serpentine asbestos (chrysotile). A similar issue can be seen with nanofibres where an amphibole structure may represent certain forms of nanofibres such as nanowires of TiO_2 or nickel formed using electrospinning or electrochemical template synthesis (e.g. see [17, 18]) yet does not reflect all forms of nanofibres. A clear example of this is carbon nanotubes which are rarely seen as perfectly straight; instead they are often curved or completely curled (and hence may present as a low-aspect-ratio compact particle like a ball of string). The bends which cause the curves are caused by topological defects in hexagonal arrangement of carbon atoms in the form of pentagons, heptagons and octagons. One of the common misconceptions of carbon nanotubes gained from this curved structure is that they are readily pliable and easy to deform; however, they are highly rigid. This curved structure (as opposed to a needle like amphibole structure) may also cause modification in depositional patterns, potentially by causing interception where an edge of the curve nanofibre contacts the airway wall.

5 Particle Retention and Relocation Pathways Within the Lungs

In general, micron-sized particles (MP) remain on the epithelial surface in airways and alveoli of rodents and are accessible to bronchoalveolar lavage (BAL) over several months of retention [19, 20]. Their retention half-lives vary between 60 and 80 days at MP doses under physiological conditions; note that retention half-lives increase drastically under particle overload conditions [21, 22].

There are only few in vivo data on the retention of NP in lung-epithelial cells or deeper in the lungs. We found 20-nm TiO_2 NP, though a small fraction, to penetrate into epithelial cells and deeper into the lung tissue within only 1 h after aerosol inhalation in rats [23]. Very few of these NPs penetrated into the blood vessels, resulting in systemic distribution and translocation of such NP into secondary organs. In this electron microscopy study, we indeed observed prominent NP accumulation within the epithelium and in the connective tissue compartments at 24 h after NP inhalation.

Accordingly, in a 6-month study with Ir NP in rats after a single 1-h inhalation, most of the inhaled 20-nm iridium NP had disappeared from the lung surface into the epithelium and into the interstitial spaces within the first day, as evidenced by the fact that the iridium NPs were no longer accessible for recovery by BAL [24, 25]. As shown in Fig. 6, 46% of the NPs could be obtained by exhaustive lung lavage immediately after the 1-h inhalation, and most of these NPs (78%) were not associated with BAL macrophages but were suspended freely in the BAL fluid. At 24 h and beyond, about 10% of the NPs were retrieved by BAL, with rapidly increasing amounts associated with lavaged macrophages such that from 72 h on, more than 90% of the lavaged NPs were associated with BAL macrophages.

To clarify whether these studies stand for differences in the materials, TiO_2 vs. Ir, to penetrate cells and epithelial barriers, we need to confirm the localization of the iridium NP at the individual particle level, i.e. by TEM, or study the biokinetics of inhaled TiO_2 NP in a quantitative approach. In fact, the latter has been achieved by radiolabelling using proton irradiation and is currently under investigation. Compared to a 10% fraction of Ir NPs totally translocated across the blood–air barrier, a significantly lower fraction of total translocated Ir NPs by a factor of 7 was observed 24 h after inhalation.

When iridium NPs were retained in the epithelium and interstitial spaces, they were accessible to lymphatic drainage. Yet, there was no noticeable NP accumulation in hilar lymph nodes surrounding the trachea and there was little NP

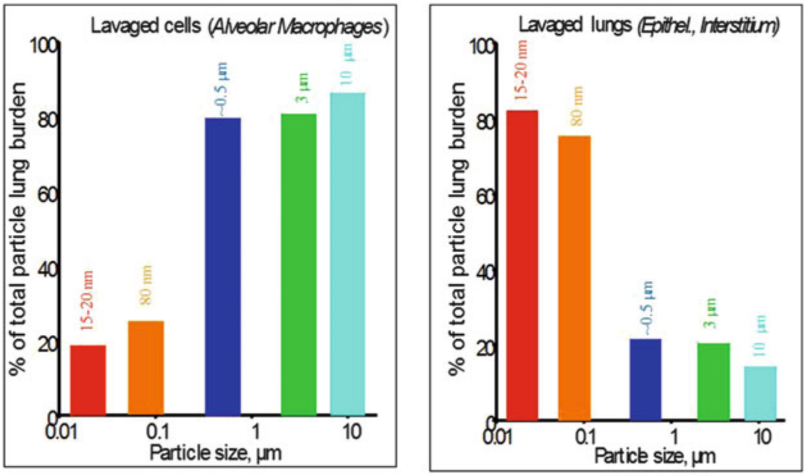

Fig. 6 Twenty-four-hour translocated fractions of alveolar NPs deposit towards blood and subsequent organs and tissues; three different materials (iridium, elemental carbon and titanium dioxide) were inhaled as freshly generated 20-nm NP aerosols for 1–2 h by healthy adult rats. The iridium NP translocation is significantly higher than those of elemental carbon and titanium dioxide NPs [55, 56]

translocation into the blood, as we found in total about 10% of the deposited NPs retained in all secondary organs and in the skeleton and soft tissue [26]. Instead, the long-term retained NPs apparently reappeared on the epithelium for subsequent clearance by lung-surface macrophages up the ciliated conducting airways towards the larynx. Although not yet clear, the most likely mechanism for NP reappearance on the epithelial surface is by macrophages. Subsequent lung-surface macrophage-mediated clearance of these NPs to the larynx is likely, since (1) more than 90% of the iridium NPs were found to be associated with BAL macrophages in any lavage performed beyond 72 h up to 6 months after aerosol inhalation and (2) almost all cleared NPs were excreted in faeces after the passage through the GI tract. Despite the initially different retention pathway of these NPs, the clearance kinetics was identical to that of MP retained on the epithelium [24, 25].

Note that the long-term retention time of MPs in the lungs of humans, monkeys and dogs is different as MPs are less retained on the epithelial surface as in rodent lungs but are much more in the interstitial tissues as discussed earlier [27–29]. Therefore, it appears plausible that in the human lungs, NPs are relocated and retained in the long term in the interstitial spaces as MPs and NPs do in rodents.

In relation to retention and clearance of fibres in the lung, length has long been seen as a critical factor in the retention and pathogenicity of fibres from the early work and development of the Stanton hypothesis [30, 31] to more recent evaluations of nanofibres [32]. A key factor here is the macrophage-mediated clearance of particles and fibres from the non-ciliated airways and the impact of length on these macrophages because where long fibres deposit in the alveolar region, these must also be dealt with by alveolar macrophages. The issue of impaired clearance occurs when a fibre is too large to be comfortably enclosed (~15 μm), yet the macrophage will still attempt (unsuccessfully) to phagocytose the fibre and becomes ‘frustrated’ [33, 34]. This frustrated phagocytosis leads to reduced mobility, failed clearance and pro-inflammatory state. An elegant example of the effect of fibre length on macrophage handling of particles and toxicity was shown by Hamilton et al. [18] who exposed macrophages to TiO2 in the form of spherical nanoparticles and short (<5 μm) or long (>15 μm) nanobelts. They found that presenting TiO2 (a relatively low toxicity material) as a long fibre structure led to a profound inflammatory response that was not observed with the shorter/non-fibrous particles of the same composition.

Most recently, Schinwald et al. [32] investigated the threshold length for fibre-induced reduced mobility in macrophages and pulmonary inflammation. By treating bone marrow-derived macrophages in culture with nanofibres of different lengths, they found that co-incubation with 5 μm silver nanowires led to slight inhibition of macrophage mobility (as assessed using the wound healing assay), yet treatment with 14 and 28 μm fibres led to substantial retardation of macrophage mobility. Aspirating these fibres into the lungs of mice showed that the shorter 3, 5 and 10 μm silver nanowires did not cause significant inflammation, yet a length-dependent inflammatory response was noted at a threshold length of 14 μm. A more recent study by Hamilton et al. [35] assessed the particle burden 7 days after exposure to a range of different carbon nanotubes that varied in size (diameter and length). They found that only the two longest MWCNT instillations resulted in significant particle retention compared to no-particle control lungs, which indicates that fibre length may have a negative impact on fibre clearance, leading to increased retention time of nanofibres.

However, nanofibres depositing in the lungs are not retained indefinitely, and translocation to other areas has been described, most often the lung-associated lymph nodes as with other low- and high-aspect-ratio particulate materials [36–38]. Whilst such translocation to the lung-associated lymph nodes is to be expected as a normal route of removal seen with micron- and nanosized particles alike, studies have also indicated that carbon nanotubes can potentially distribute more widely. In their 2013 publication, Mercer et al. exposed mice via inhalation to carbon nanotubes to assess their distribution to extrapulmonary sites. They found that the tracheobronchial lymph nodes contained 1.08% of the lung burden at 1 day and 7.34% at 336 days postexposure [39]. They also found carbon nanotubes in the diaphragm, chest wall, liver, kidney, heart and brain with an average of 15,371 fibres per gram of tissue at 1 day and an increased level of 109,885 fibres at 336 days postexposure. Interestingly they found that agglomerates of carbon nanotubes accounted for approximately 54% of lung burden, yet only singlet carbon nanotubes were noted in extrapulmonary regions [39] indicating that agglomerated carbon nanotubes may be hindered by their shape/size from translocating widely. To put the level of extrapulmonary transport into context, the authors expressed the number of fibres translocated to the extrapulmonary organs relative to the initial number of fibres deposited in the lungs at 1 day postexposure and found that at day 1, approximately 1 fibre deposits in an extrapulmonary organ for every 25,700 fibres of lung burden being transported to extrapulmonary tissues [39].

This extrapulmonary transport has important safety connotations, particularly where there is the potential for accumulation of dose with repeated exposures. One such site of particular concern is the retention and effect of nanofibres such as carbon nanotubes on the pleura and specifically the development of mesothelioma, a uniformly fatal cancer of the pleural lining (the mesothelium) which is almost exclusively associated with exposure to specific pathogenic fibres (e.g. erionite, asbestos) [33, 34]. Mercer and colleagues have demonstrated in several studies that carbon nanotubes depositing in the lungs can and do transfer to the pleural space [39, 40], indicating that a pleural dose of these nanofibres is indeed possible, and others have also shown that lung-deposited carbon nanotubes can elicit a response in the sub-pleural and pleural space [41, 42]. Such pleural penetrations of nanofibres are not unexpected as the transit of deposited material from the lung to the pleura is neither new nor specific to fibres; indeed postmortem studies have shown the common presence of particle accumulations or ‘black spots’ in the parietal pleura of individuals exposed to a repeated high particle concentration (e.g. urban dwellers, coal miners) [43]. However, the potential for retention and causation of a pathogenic effect due to fibre length preventing pleural clearance to the mediastinal lymph nodes has been a concern for some time [44]. Several studies have now shown length-dependent retention of nanofibres in the pleural space and the subsequent development of acute pleural inflammation and fibrosis [17, 44–46], and recently, Schinwald et al. [47] identified a threshold length for nanofibre-induced pleural inflammation of 5 µm. Similar to the threshold for pulmonary inflammation, this length threshold reflects the clearance mechanisms of the pleural cavity which are twofold. The route is in the flow of pleural fluid out of the pleural space into the lymphatic system (to the mediastinal lymph nodes) through stomata openings located in the parietal pleura which are 2–8 μm in diameter [48]. If a fibre is longer than the diameter of the stomata, it will most likely be retained at the mesothelial surface where it may cause a reaction. The second mechanism of clearance is by the action of resident pleural macrophages, but these are likely to have the same difficulties as the alveolar macrophages and become ‘frustrated’.

As the evidence has shown, lung-depositing carbon nanotubes (and possibly other nanofibres) can penetrate through to the pleural cavity and, with sufficient length, frustrate normal clearance and be retained and cause an inflammatory/fibrotic response. The key question therefore remains: can they cause mesothelioma? Rittinghausen and colleagues [49] exposed rats by intraperitoneal injection (a surrogate for pleural exposure although bypasses the lung defences) to four carbon nanotube samples with WHO dimensions. They found that all of the carbon nanotube samples caused mesothelioma, and they observed the highest frequencies and the earliest appearances of mesothelioma with the rather straight carbon nanotube samples. Taken together, the exposure, translocation, retention and effect of exposure to carbon nanotube which meet the criteria of a pathogenic fibre (e.g. length, diameter and biodurability) appear to mirror that of other pathogenic fibres. It should be considered that the above discussion does not address the other key modification of fibre-induced pathogenicity and retention, and that is biodurability. If a fibre is retained in the alveolar region and cannot be cleared by the actions of alveolar macrophages, another route of removal is the dissolution and disintegration of the fibre in lung-lining fluid (as commonly seen with certain soluble MMVF [50]). Where fibres show low biodurability (e.g. glass fibre), their dissolution in the lung leads to a progressive removal of dose, yet where fibres have high durability (e.g. amphibole asbestos), they may persist. This role of fibre durability in pathogenesis is equally applicable to nanofibres such as carbon nanotubes; variance in biodurability has been indicated [51, 52], but overall the material is considered to be durable.

6 Extrapolation from Single Dose to Chronic Exposure

Recently we have extrapolated NP accumulations in secondary organs after 1 year of assumed chronic exposure [3]. These estimates were based on daily doses of ambient insoluble NP. The daily dose of insoluble NP to the human lung can be estimated from the following assumptions:

10^3 cm^{-3} insoluble NP in inhaled air, i.e. 10% of an average NP concentration of 10^4 cm^{-3}
10^4 L daily inhaled gas volume by an adult human
30% deposited fraction of the inhaled NP in the peripheral lungs

3×10^9 daily dose of deposited insoluble NP in the human lung

3×10^{11} long-term retained NP in the lung during 1 year exposure (assuming about 30% clearance of these insoluble NPs from the lungs [28])

Based on these assumptions, 6×10^{8} NP would have accumulated in each secondary target organ during 1 year of continuous exposure. Although the accumulated doses in secondary organs are three orders of magnitude below the lung dose, they are indeed not negligible when considering their number whilst their mass is very low.

Besides the discussed importance of size and material, other NP characteristics such as surface charge (zeta potential) and other surface properties are very likely to influence the NP biokinetics. They determine the interactions of NP with proteins and cellular components and thereby the transport mechanisms responsible for NP translocation and accumulation in extrapulmonary organs as well as potential health effects. However, it needs to be emphasized that according to the current knowledge, NP translocation to and accumulation in extrapulmonary organs are a minor clearance pathway for NP from the lungs compared to alveolar and airway macrophage-mediated NP clearance towards the larynx. Yet, whilst the latter pathway leads to NP elimination via the gastrointestinal tract, NP translocation into the blood circulation distributes NP in the body and may target and result in adverse effects in sensitive target organs such as the cardiovascular system, the central nervous system and the immune system. Despite the potential toxicological consequences for the organism when NPs interact with these organ systems, it is still unknown whether translocated NPs directly cause adverse effects that have been observed in epidemiological studies of particulate air pollution. Particularly, it remains to be shown whether chronic exposure leads to sufficiently high NP doses to trigger or mediate responses leading to initiation and/or progression of disease. In addition, the release of mediators into the blood circulation needs thorough investigations: these mediators may be released via induction of oxidative stress which is a well-established response to NP [53, 54].

Inhaled nanoparticles depositing throughout the respiratory tract can, depending on the size and surface properties (e.g. charge, primary and secondary coatings with proteins, lipids and functional groups), translocate across epithelial barriers and along sensory neuronal pathways to reach secondary organs and tissues such as the vascular endothelium, the heart and the brain. Effects induced in these tissues may be due either to a direct effect by the nanoparticles retained at these sites, by mediators induced by the nanoparticles at the portal of entry and released into the circulation or a combination of both or via neuronal signals.

An additional area of consideration for extrapolation from single dose to chronic dose is considering the overall experimental design and, in particular, the length of the postexposure period. Low-level exposure (reflecting many occupation exposures) to particles may not necessarily demonstrate a prominent acute response, yet a lack of such response does not confirm a particle or fibre is benign. Indeed certain disease states (e.g. mesothelioma) have a considerable lag time between exposure and the onset of disease and so postexposure periods should be of sufficient duration (to the extent possible) to detect more chronic effects. Another reason behind coupling short-term exposure with longer-term postexposure periods is to assess how an effect (e.g. inflammation) progresses and in particular resolves or is maintained which can have important implications for risk assessment.

7 Toxicity

There are several theories regarding the toxicity of nanomaterial and how it may differ from larger inhaled particles. Toxicity will depend on the chemical composition, internal structure and particle size that elicit a unique carrier transport [57]. High particle number, overall large surface areas and high lung deposition efficiency due to small size may also be important in contributing to the health effects [58, 59]. The latter results in a higher dose at a similar exposure concentration compared to that of micron-sized particles. Due to their physicochemical properties that give them enhanced features [60], manufactured nanoparticles may be biopersistant and remain intact and cause and/or mediate toxicity.

One major difference between micron- and nanosized particles is the different recognition patterns between alveolar macrophages that have an essential role in clearing particles from the lungs and the epithelial cells, with their function being predominantly the facilitation of gas exchange between the air and the blood (oxygen and carbon dioxide). As illustrated in fig. 6, macrophages may not recognize nano sized particles efficiently which results in a higher dose for the epithelial cells.

Plausible biological mechanisms linking airborne nanomaterials pollution to cardiovascular disease involve (a) direct effects of pollutants on cardiac, endothelial, blood and pulmonary cells and receptors and/or (b) indirect effects mediated through pollutant-induced pulmonary oxidative stress and inflammatory responses and/or (c) activation of the autonomous nervous system. Direct effects may occur via agents that readily cross the pulmonary epithelium into the circulation, such as gases, and ultrafine particles along with soluble constituents of PM2.5 (e.g. transition metals). In addition, activation of the autonomous nervous system secondary to PM interactions with sensory neurons and receptors in the airways may play a role. These direct effects of airborne nanomaterials represent a conceivable explanation for the occurrence of rapid (within a few hours) cardiovascular responses, such as onset of myocardial infarctions in predisposed people. In contrast, less acute (several hours to days) and chronic indirect effects may occur via pulmonary oxidative stress/inflammation and build-up of morphological changes induced by inhaled pollutants. Nanomaterials have been suggested to directly interact with target cells and cross cell barriers. Apart from crossing the lung–blood barrier, evidence is emerging that nanoparticles deposit on the olfactory epithelium in the nose and can relocate into the various parts of the brain via the olfactory bulb.

Once nanomaterials are blood-borne, they will be transported to other parts of the body, whereas the liver and the spleen act as efficient filtration systems.

However, the latter may also respond with a pro-inflammatory response as can be seen in the lung after exposure to nanomaterials. So the majority of inhalation toxicity studies suggest that the effect of granular nanomaterials is largely driven by the dissolution rate in the case of (transition) metals, whereas the adverse responses due to exposure to fibres are highly dependent on the aspect ratio and sometimes can result in asbestos-like effects when fibres are rigid and biopersistent (as discussed above).

References

1. Oberdörster G, Maynard A, Donaldson K, Castranova V, Fitzpatrick J, Ausman K, Carter J, Karn B, Kreyling W, Lai D, Olin S, Monteiro-Riviere N, Warheit D, Yang H, ILSI Research Foundation/Risk Science Institute Nanomaterial Toxicity Screening Working Group (2005) Principles for characterizing the potential human health effects from exposure to nanomaterials: elements of a screening strategy. Part Fibre Toxicol 2:8
2. Kreyling WC, Semmler-Behnke M, Möller W (2006) Health implications of nanoparticles. J Nano Res 8:543–562
3. Kreyling WG, Möller W, Semmler-Behnke M, Oberdörster G (2007) Particle dosimetry: deposition and clearance from the respiratory tract and translocation towards extra-pulmonary sites. In: Donaldson K, Borm P (eds) Particle toxicology. CRC/Taylor & Francis, Boca Raton
4. Möller W, Kreyling WG, Schmid O, Semmler-Behnke M, Schulz H (2009) Deposition, retention and clearance, and translocation of inhaled fine and nano-sized particles in the respiratory tract. In: Gehr P, Blank F, Mühlfeld C, Rothen-Rutishauser B (eds) Particle-lung interactions, 2nd edn. Informa Healthcare, New York
5. Kingma PS, Whitsett JA (2006) In defense of the lung: surfactant protein A and surfactant protein D. Curr Opin Pharmacol 6(3):277–283
6. Lynch I, Cedervall T, Lundqvist M, Cabaleiro-Lago C, Linse S, Dawson KA (2007) The nanoparticle-protein complex as a biological entity; a complex fluids and surface science challenge for the 21st century. Adv Colloid Interface Sci 134–135:167–174
7. Treuel L, Docter D, Maskos M, Stauber RH (2015) Protein corona – from molecular adsorption to physiological complexity. Beilstein J Nanotechnol 6:857–873
8. Cho WS, Duffin R, Thielbeer F, Bradley M, Megson IL, Macnee W, Poland CA, Tran CL, Donaldson K (2012) Zeta potential and solubility to toxic ions as mechanisms of lung inflammation caused by metal/metal-oxide nanoparticles. Toxicol Sci 126(2):469–477
9. Oberdörster G (1996) Significance of particle parameters in the evaluation of exposure-dose-response relationships of inhaled particles. Inhal Toxicol 8(Suppl):73–89
10. Asgharian B, Hofmann W, Bergmann R (2001) Particle deposition in a multiple-path model of the human lung. Aerosol Sci Technol 34:332–339
11. WHO (1997) Determination of airborne fibre number concentrations. A recommended method, by phase-contrast optical microscopy membrane filter method. World Health Organization, Geneva
12. Brown J, Gordon T, Price O, Asgharian B (2013) Thoracic and respirable particle definitions for human health risk assessment. Part Fibre Toxicol 10(1):12
13. Morgan A (1995) Deposition of inhaled asbestos and man-made mineral fibres in the respiratory tract. Ann Occup Hyg 39(5):747–758
14. Balashazy I, Moustafa M, Hofmann W, Szoke R, El-Hussein A, Ahmed AR (2005) Simulation of fiber deposition in bronchial airways. Inhal Toxicol 17(13):717–727
15. Jones AD (1993) Respirable industrial fibres: deposition, clearance and dissolution in animal models. Ann Occup Hyg 37(2):211–226

16. Sturm R, Hofmann W (2009) A theoretical approach to the deposition and clearance of fibers with variable size in the human respiratory tract. J Hazard Mater 170(1):210–218
17. Poland C, Byrne F, Cho W, Prina-Mello A, Murphy F, Davies G (2011) Length-dependent pathogenic effects of nickel nanowires in the lungs and the peritoneal cavity. Nanotoxicology 6:899
18. Hamilton RF, Wu N, Porter D, Buford M, Wolfarth M, Holian A (2009) Particle length-dependent titanium dioxide nanomaterials toxicity and bioactivity. Part Fibre Toxicol 6:35
19. Lehnert BE, Valdez YE, Tietjen GL (1989) Alveolar macrophage-particle relationships during lung clearance. Am J Respir Cell Mol Biol 1(2):145–154
20. Ellender M, Hodgson A, Wood KL, Moody JC (1992) Effect of bronchopulmonary lavage on lung retention and clearance of particulate material in hamsters. Environ Health Perspect 97: 209–213
21. Morrow PE (1988) Possible mechanisms to explain dust overloading of the lungs. Fundam Appl Toxicol 10(3):369–384
22. Morrow PE (1992) Dust overloading of the lungs: update and appraisal. Toxicol Appl Pharmacol 113(1):1–12
23. Geiser M, Rothen-Rutishauser B, Kapp N, Schurch S, Kreyling W, Schulz H, Semmler M, Im Hof V, Heyder J, Gehr P (2005) Ultrafine particles cross cellular membranes by nonphagocyticmechanisms in lungs and in cultured cells. Environ Health Perspect 113:1555–1560
24. Semmler M, Seitz J, Erbe F, Mayer P, Heyder J, Oberdörster G, Kreyling WG (2004) Long-term clearance kinetics of inhaled ultrafine insoluble iridium particles from the rat lung, including transient translocation into secondary organs. Inhal Toxicol 16(6–7):453–459
25. Semmler-Behnke M, Takenaka S, Fertsch S, Wenk A, Seitz J, Mayer P, Oberdörster G, Kreyling WG (2007) Efficient elimination of inhaled nanoparticles from the alveolar region: evidence for interstitial uptake and subsequent reentrainment onto airways epithelium. Environ Health Perspect 115(5):728–733
26. Kreyling WG, Semmler-Behnke M, Seitz J, Scymczak W, Wenk A, Mayer P, Takenaka S, Oberdorster G (2009) Size dependence of the translocation of inhaled iridium and carbon nanoparticle aggregates from the lung of rats to the blood and secondary target organs. Inhal Toxicol 21:55–60
27. Nikula KJ, Avila KJ, Griffith WC, Mauderly JL (1997) Sites of particle retention and lung tissue responses to chronically inhaled diesel exhaust and coal dust in rats and cynomolgus monkeys. Environ Health Perspect 105(Suppl 5):1231–1234
28. Kreyling WG, Scheuch G (2000) Clearance of particles deposited in the lungs. In: Gehr P, Heyder J (eds) Particle-lung interactions. Marcel Dekker, New York/Basel, pp 323–376
29. Kreyling WG, Semmler-Behnke M, Takenaka S, Moller W (2013) Differences in the biokinetics of inhaled nano- versus micrometer-sized particles. Acc Chem Res 46:714–722
30. Stanton MF, Laynard M, Tegeris A, Miller E, May M, Kent E (1977) Carcinogenicity of fibrous glass: pleural response in the rat in relation to fiber dimension. J Natl Cancer Inst 58(3):587–603
31. Stanton M, Layard M, Tegeris A, Miller E, May M, Morgan E (1981) Relation of particle dimension to carcinogenicity in amphibole asbestoses and other fibrous minerals. J Natl Cancer Inst 67:965–975
32. Schinwald A, Chernova T, Donaldson K (2012) Use of silver nanowires to determine thresholds for fibre length-dependent pulmonary inflammation and inhibition of macrophage migration in vitro. Part Fibre Toxicol 9(1):47
33. Donaldson K, Murphy FA, Duffin R, Poland CA (2010a) Asbestos, carbon nanotubes and the pleural mesothelium: a review and the hypothesis regarding the role of long fibre retention in the parietal pleura, inflammation and mesothelioma. Part Fibre Toxicol 7(1):5
34. Donaldson K, Murphy F, Duffin R, Poland C (2010b) Asbestos, carbon nanotubes and the pleural mesothelium: a review of the hypothesis regarding the role of long fibre retention in the parietal pleura, inflammation and mesothelioma. Part Fibre Toxicol 7(5):5

35. Hamilton RF Jr, Wu Z, Mitra S, Shaw PK, Holian A (2013) Effect of MWCNT size, carboxylation, and purification on in vitro and in vivo toxicity, inflammation and lung pathology. Part Fibre Toxicol 10(1):57
36. Ellinger-Ziegelbauer H, Pauluhn J (2009) Pulmonary toxicity of multi-walled carbon nanotubes (Baytubes) relative to alpha-quartz following a single 6h inhalation exposure of rats and a 3 months post-exposure period. Toxicology 266(1–3):16–29
37. Pauluhn J (2010) Subchronic 13-week inhalation exposure of rats to multiwalled carbon nanotubes: toxic effects are determined by density of agglomerate structures, not fibrillar structures. Toxicol Sci 113(1):226–242
38. Ma-Hock L, Strauss V, Treumann S, Kuttler K, Wohlleben W, Hofmann T, Groters S, Wiench K, van Ravenzwaay B, Landsiedel R (2013) Comparative inhalation toxicity of multi-wall carbon nanotubes, graphene, graphite nanoplatelets and low surface carbon black. Part Fibre Toxicol 10(1):23
39. Mercer RR, Scabilloni JF, Hubbs AF, Wang L, Battelli LA, McKinney W, Castranova V, Porter DW (2013) Extrapulmonary transport of MWCNT following inhalation exposure. Part Fibre Toxicol 10(1):38
40. Mercer RR, Hubbs AF, Scabilloni JF, Wang L, Battelli LA, Schwegler-Berry D, Castranova V, Porter DW (2010) Distribution and persistence of pleural penetrations by multi-walled carbon nanotubes. Part Fibre Toxicol 7:28
41. Ryman-Rasmussen JP, Cesta MF, Brody AR, Shipley-Phillips JK, Everitt JI, Tewksbury EW, Moss OR, Wong BA, Dodd DE, Andersen ME, Bonner JC (2009) Inhaled carbon nanotubes reach the subpleural tissue in mice. Nat Nanotechnol 4(11):747–751
42. Murphy FA, Poland CA, Duffin R, Donaldson K (2013) Length-dependent pleural inflammation and parietal pleural responses after deposition of carbon nanotubes in the pulmonary airspaces of mice. Nanotoxicology 7:1157–1167
43. Mitchev K, Dumortier P, De VP (2002) 'Black Spots' and hyaline pleural plaques on the parietal pleura of 150 urban necropsy cases. Am J Surg Pathol 26(9):1198–1206
44. Poland CA, Duffin R, Kinloch I, Maynard A, Wallace WA, Seaton A, Stone V, Brown S, Macnee W, Donaldson K (2008) Carbon nanotubes introduced into the abdominal cavity of mice show asbestos-like pathogenicity in a pilot study. Nat Nanotechnol 3(7):423–428
45. Murphy F, Poland C, Duffin R, Al-Jamal K, Ali-Boucetta H, Nunes A (2011) Length-dependent retention of carbon nanotubes in the pleural space of mice initiates sustained inflammation and progressive fibrosis on the parietal pleura. Am J Pathol 178:2587–2600
46. Murphy FA, Schinwald A, Poland CA, Donaldson K (2012) The mechanism of pleural inflammation by long carbon nanotubes: interaction of long fibres with macrophages stimulates them to amplify pro-inflammatory responses in mesothelial cells. Part Fibre Toxicol 9:8
47. Schinwald A, Murphy F, Prina-Mello A, Poland C, Byrne F, Movia D (2012) The threshold length for fiber-induced acute pleural inflammation: shedding light on the early events in asbestos-induced mesothelioma. Toxicol Sci 128:461–470
48. Tsilibary EC, Wissig SL (1977) Absorption from the peritoneal cavity: SEM study of the mesothelium covering the peritoneal surface of the muscular portion of the diaphragm. Am J Anat 149(1):127–133
49. Rittinghausen S, Hackbarth A, Creutzenberg O, Ernst H, Heinrich U, Leonhardt A, Schaudien D (2014) The carcinogenic effect of various multi-walled carbon nanotubes (MWCNTs) after intraperitoneal injection in rats. Part Fibre Toxicol 11(1):59
50. Hesterberg TW, Hart GA, Chevalier J, Miiller WC, Hamilton RD, Bauer J, Thevenaz P (1998) The importance of fiber biopersistence and lung dose in determining the chronic inhalation effects of X607, RCF1, and chrysotile asbestos in rats. Toxicol Appl Pharmacol 153(1):68–82
51. Kagan VE, Konduru NV, Feng W, Allen BL, Conroy J, Volkov Y, Vlasova II, Belikova NA, Yanamala N, Kapralov A, Tyurina YY, Shi J, Kisin ER, Murray AR, Franks J, Stolz D, Gou P, Klein-Seetharaman J, Fadeel B, Star A, Shvedova AA (2010) Carbon nanotubes degraded by neutrophil myeloperoxidase induce less pulmonary inflammation. Nat Nanotechnol 5:354–359

52. Osmond-McLeod MJ, Poland CA, Murphy F, Waddington L, Morris H, Hawkins SC, Clark S, Aitken R, McCall MJ, Donaldson K (2011) Durability and inflammogenic impact of carbon nanotubes compared with asbestos fibres. Part Fibre Toxicol 8
53. Donaldson K, Stone V, Borm PJ, Jimenez LA, Gilmour PS, Schins RP, Knaapen AM, Rahman I, Faux SP, Brown DM, MacNee W (2003) Oxidative stress and calcium signaling in the adverse effects of environmental particles (PM10). Free Radic Biol Med 34(11): 1369–1382
54. Donaldson K, Borm PJ, Castranova V, Gulumian M (2009) The limits of testing particle-mediated oxidative stress in vitro in predicting diverse pathologies; relevance for testing of nanoparticles. Part Fibre Toxicol 6:13
55. Oberdörster G (2001) Pulmonary effects of inhaled ultrafine particles. Int Arch Occup Environ Health 74(1):1–8
56. Kreyling WG, Semmler M, Erbe F, Mayer P, Takenaka S, Schulz H, Oberdörster G, Ziesenis AJ (2002) Translocation of ultrafine insoluble iridium particles from lung epithelium to extrapulmonary organs is size dependent but very low. Toxicol Environ Health A 65 (20):1513–1530
57. Johnston CF, Finkelstein JN, Mercer P, Corson N, Gelein R, Oberdörster G (2000) Pulmonary effects induced by ultrafine PTEF particles. Toxicol Appl Pharmacol 168:208–215
58. Oberdörster G, Gelein RM, Ferin J, Weiss B (1995) Association of particulate air pollution and acute mortality: involvement of ultrafine particles. Inhal Toxicol 7:111–124
59. Utell MJ, Frampton MW (2000) Who is susceptible to particulate matter and why? Inhal Toxicol 12(Suppl 1):37–40
60. Maynard AD, Baron PA, Foley M, Shedova AA, Kisin ER, Castranova V (2004) Exposure to carbon nanotube material: aerosol release during the handling of unrefined single-walled carbon nanotube material. J Toxicol Environ Health A 67:87–107

Measurement Methods for Nanoparticles in Indoor and Outdoor Air

Christof Asbach, Simon Clavaguera, and Ana Maria Todea

Abstract A large variety of measurement methods for the characterization of airborne nanoparticles in indoor or outdoor air exist. The choice of an appropriate method depends strongly on the questions to be tackled. If the aerosol is to be characterized only for a single location, one may use stationary equipment that is rather bulky but provides the most details and is most accurate. Spatially resolved measurements can only be conducted with portable or personal measurement equipment which provide a limited dataset with lower accuracy. Furthermore, the metrics to be measured (e.g., number, surface area of mass concentration, chemical composition, etc.) determine the choice of measurement methods as no single method can do it all. Another determining factor is the time resolution of the instruments. While direct-reading monitors deliver the information with high time resolution (often 1 s) and hence allow for linking the measured concentration to certain activities, samplers collect the particles for subsequent analyses and therefore provide an average over the sampling time. Consequently, the choice of a measurement instrument for the characterization of airborne nanoparticles remains a compromise. In many practical applications, the combination of different techniques may be required.

Keywords Indoor Air, Outdoor Air, Air Quality, Nanoparticles, Exposure, Aerosol Measurement

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1 Introduction

Nanoparticles are ubiquitous in indoor and outdoor air. They can stem from a large variety of sources. According to the definition of the European Commission, a nanomaterial is "a natural, incidental or manufactured material containing particles, in an unbound state or as an aggregate or as an agglomerate and where, for 50 % or more of the particles in the number size distribution, one or more external dimensions is in the size range 1–100 nm" [1]. Nanomaterials can hence be intentionally produced synthetic particles which are used in numerous applications such as cosmetics, coatings, or tires; they can be by-products from human activities, e.g., soot from incomplete combustion; or they can be naturally produced particles, e.g., sea salt from ocean mist or nucleation particles. Although it may not be strictly correct, the term nanoparticle is used synonymously with nanomaterial according to the EC definition here. In the past, several studies have shown that nanoparticles may cause more severe biological effects than the same mass dose of larger particles of identical chemical entity [2–4]. The assessment of exposure to airborne nanoparticles in both indoor and outdoor environments has therefore raised increased attention in the recent years. The traditional exposure assessment focused on wider size fractions, e.g., all particles below 10 μm (PM_{10}) or 2.5 μm ($PM_{2.5}$) in ambient measurements or below 4 μm (respirable fraction) in workplace exposure assessment. These measurements determine the total mass concentration of the respective particle size fraction. The mass concentration scales with the third power of the particle diameter and therefore weights larger particles much more strongly than smaller ones. As an example, a single 10 μm particle has the same mass as one thousand 1 μm particles, one million 100 nm particles, or one billion 10 nm particles. Although nanoparticles typically occur in much higher numbers than micron-sized particles, it is obvious that they usually only contribute a very small fraction to the total mass concentration. To obtain a better representation of the presence of nanoparticles, metrics other than the mass concentration are therefore required. An example for a bimodal particle size distribution is shown in Fig. 1. The graph shows the same size distribution, represented as number size distribution, surface area size distribution, and mass size distribution. Both modes of the distribution are lognormal. The first mode has a count median diameter (CMD) of 100 nm, a geometric standard deviation (σ_g) of 1.7, and a total number concentration of 500,000 $1/\text{cm}^3$, and the second mode has a CMD of 3,000 nm, a σ_g of 2.0,

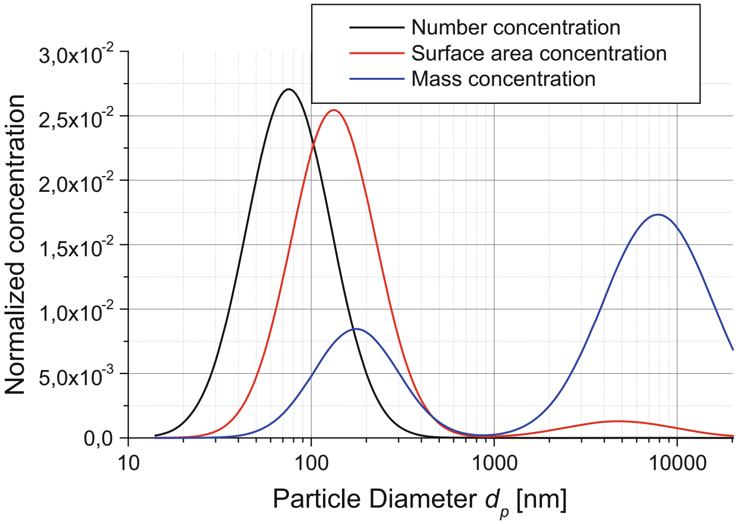


Fig. 1 Example for a bimodal particle size distribution; first mode with a CMD at 100 nm and 500,000 1/cm^3 and second mode with CMD at 3,000 nm (3 μm) and 1,000 1/cm^3, represented as number size distribution (*black*), surface area size distribution (*red*), and mass size distribution (*blue*); for clearer representation, all data have been normalized with respect to the total concentration

and a total number concentration of 1,000 1/cm^3. For better representation, the graphs have been normalized to the respective total concentration. The figure shows that in the number size distribution the second mode is invisible, due to its low number concentration, whereas it contributes the major part to the mass size distribution. In the surface area size distribution, the first mode is still dominant, but the second mode is clearly visible. The surface area concentration has raised increased attention in the recent years, because several studies indicated that the biological effects seem to correlate best with the total particle surface area dose [3, 5]. Currently, no instrument exists that is capable of measuring the particle surface area concentration of airborne particles. The only surface area-related metric that can be measured is the lung-deposited surface area (LDSA) concentration, i.e., the fraction of the total airborne surface area concentration that upon inhalation would be retained in the human lung.

Besides the particle size, the particle morphology and chemical composition can also play a significant role in the toxicity of inhaled particles. It was, for example, shown that the effects of CeO_2 particles were significantly higher than that of TiO_2 particles for the same mass dose and similar particle sizes. On the contrary, $BaSO_4$ particles produced no noticeable effects [6]. Poland et al. [7] found that carbon nanotubes (CNTs) can have asbestos-like effects, but only if they are stiff and have a high aspect ratio and occur as a single CNT and not in bundles.

The available instrumentation to assess exposure to nanoparticles can be differentiated into stationary, portable, and personal equipment. Furthermore, it can be differentiated into (quasi-)real-time instruments that deliver the results with high time resolution and particle samplers that collect particles for subsequent chemical and/or morphological analyses.

Stationary equipment is typically the most accurate but only gives information for a single measurement location. In workplace exposure assessment, stationary equipment is mainly used for tier 3 measurements. The instruments are mains powered and bulky so that the transport to another location requires quite some effort. Portable instruments are much smaller and battery operated so that they can easily be moved from one location to another, i.e., they are most suitable for tier 2 measurements in workplace exposure assessment. Their accuracy and sizing resolution (if applicable) are typically lower than for stationary instruments. Personal instruments are small enough to be carried by a person and measure/sample in the breathing zone, i.e., within a 30 cm hemisphere around the mouth and nose of the individual [8] in order to measure the true personal exposure. The choice of an instrument or a suite of instruments always remains a compromise between the size of the instrument(s) on the one side and the wealth and quality of the data on the other side. If the intention is to obtain a best possible characterization of the aerosol, then a large set of equipment is required that is immobile and expensive but provides the most detailed analysis with high accuracy. In contrast, if the intention is to keep track of the exposure of an individual, then only small, person-carried instruments come into play, which however only deliver a limited dataset with lower accuracy.

The intention of this book chapter is to provide an overview of the existing measurement methods for nanoparticles, their typical field of application, as well as their strengths and weaknesses.

2 Measurement Methods

This section provides the details on the measurement methods and instruments used for the quantification of airborne nanoparticles. The description starts with the stationary equipment which comprises the most accurate instruments. Portable and personal instruments were developed later than the stationary instruments and use the same or similar techniques. The instrument groups are further differentiated into time-resolving (real-time) instruments and time-integrating (sampling) instruments. While the time-resolving instruments all use measurement methods specific for a certain metric, time-integrating instruments sample particles on substrates which can be analyzed for different purposes, e.g., morphology or chemical composition.

2.1 Stationary Equipment

Stationary equipment is characterized by the instrument size, which is typically bulky, and its need for mains power, which immobilizes the equipment. The equipment is furthermore differentiated into time resolving and time integrating. Time-resolving instruments are those that deliver the results in (quasi-)real time with high time resolution, whereas time-integrating instruments sample the particles onto substrates or filters for subsequent analyses of the chemical composition or the particle morphology. The time-integrated results can be either qualitative (e.g., proof for the presence or absence of a certain particle morphology like CNTs) or quantitative as an average of the sampling time. Stationary equipment is typically most accurate and provides the highest size resolution (if applicable) and therefore used for detailed aerosol analyses like in tier 3 workplace exposure assessment.

2.1.1 Time-Resolving Instruments

Measurement of Particle Number Concentration

Only particles larger than approximately half the wavelength of light can be detected optically. Conventional optical particle counters therefore only detect particles down to approximately 250 nm and are not further covered here. Condensation particle counters (CPCs) artificially enlarge the particles to make them optically detectable. As shown in Fig. 2, the incoming aerosol is first guided through a heated saturator, in which a working fluid (usually butanol, isopropyl alcohol, or water) is evaporated until the air is saturated with vapor. Typical sampling flow rates are between 0.3 and 1.5 L/min. In the following condenser, the temperature is reduced, resulting in a supersaturation of the working fluid vapor. The particles now act as condensation nuclei, i.e., vapor condenses onto the particle surfaces and the aerosol leaving the condenser contains only droplets with the original particles inside. Since the vapor is homogenously distributed onto all particles, each droplet represents exactly one particle so that counting of the droplets in the downstream optical sensor also yields the number (concentration) of the particles in the incoming aerosol. Growth factors between the original particle diameter and the eventual droplet diameter between 100 and 1,000 are common [9]. The eventual droplet size distribution is, however, quite narrow, therefore facilitating two different particle count modes. The most common one is the single particle count mode, where each single light-scattering event of a particle in the optical sensor is counted individually. The single particle count mode breaks down at high concentration, where two or more particles may simultaneously be present in the sensor, resulting in a single combined light-scattering event. The two or more particles in the sensor would therefore be counted as a single particle, resulting in too low particle number concentrations reported by the CPC. This phenomenon is known as coincidence error. Depending on the CPC

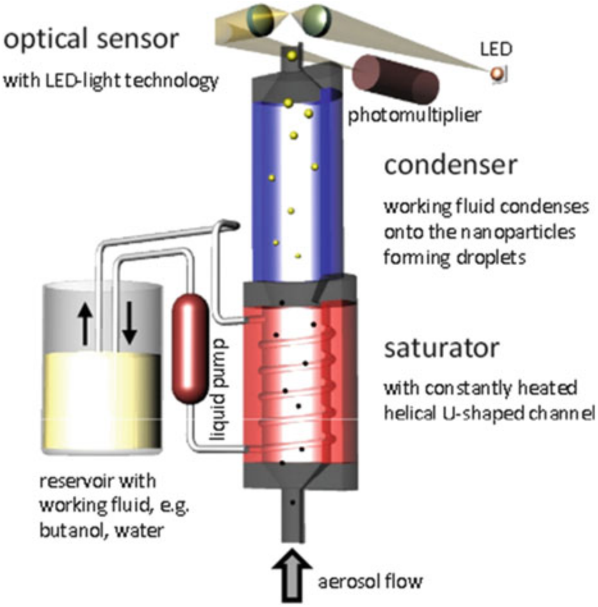


Fig. 2 Schematic of a condensation particle counter (CPC, image courtesy of Palas GmbH)

model, the upper concentration limit for the single particle count mode is typically between around 50,000 1/cm^3 and 300,000 1/cm^3, although some higher and lower exceptions apply. For higher concentrations, some instruments switch to a so-called photometric mode. In the photometric mode, the total light scattered by all particles in the optical sensor is quantified. If all droplets have the same size and refractive index, then each particle scatters the same amount of light and therefore the particle number concentration can be determined. The photometric mode extends the concentration range of a CPC up to between one and ten million particles per cubic centimeter. A prerequisite for the photometric particle count mode is that the droplet size is known and ideally material independent. The latter can only be assumed for alcoholic working fluids, whereas it was shown that the eventual droplet size in water-based CPCs can vary drastically in case of hydrophobic and hydrophilic particles [10]. If an average, material-independent droplet size is assumed for the calibration of water-based CPCs, the concentration measurements can be significantly biased.

The lowest particle sizes that can be detected with modern CPCs are between 2.5 and 10 nm (depending on model). For alcohol-based CPCs, the lower size limit only weakly depends on the particle material, whereas the activation of small particles with water vapor is different for hydrophilic and hydrophobic particles. The upper size limit of CPCs is usually not well specified. While in principle micron-sized particles would be more easily detectable in the sensor, they also get more easily lost in the instrument due to inertia or sedimentation. Most manufacturers therefore specify the upper limit as 1 μm, although there is no strict reason for a clear cutoff. It should, however, be noted that the number concentration of micron-sized particles is typically very low (see Fig. 1). CPC instruments are available from several manufacturers including (in alphabetical order) Grimm Aerosol (Ainring, Germany), HCT (Korea), Palas (Karlsruhe, Germany), and TSI Inc. (Shoreview, MN, USA).

Measurement of Particle Lung-Deposited Surface Area Concentration

The lung-deposited surface area (LDSA) concentration is the only surface area-related metric that can currently be measured directly. The LDSA concentration is the fraction of the airborne particle surface area concentration that upon inhalation would deposit in the human lung. The LDSA concentration can be determined by measuring the number size distribution, weighting it with the particle surface area, i.e., πd_p^2 (see surface area size distribution in Fig. 1), and the lung deposition efficiency, before integrating it over the particle size range of interest. The lung deposition efficiency can be obtained for different compartments of the human lung from sampling conventions [11] or a model [12]. Since it is dependent on individual physiological and breathing parameters, a parameter set has been defined for a "reference worker" in order to make data comparable [13]. Available instruments determine the fraction that would deposit either in the alveolar or tracheobronchial region of the lung.

The first instrument to measure the LDSA concentration was the Nanoparticle Surface Area Monitor (NSAM, TSI model 3550) [13, 14]. The instrument is depicted in Fig. 3 and is to date the only stationary instrument that determines this metric. The aerosol is taken in at a flow rate of 2.5 L/min and passes a cyclone with 1 μm cutoff (not shown in the figure), before it is split into a 1 L/min ion jet flow and a 1.5 L/min aerosol flow. The ion jet flow passes a corona needle with an applied voltage of +2.5 kV. The high voltage at the corona tip establishes a corona discharge which generates ions. These ions are transported convectively with the ion jet flow into a mixing chamber, where it is recombined with the aerosol flow. Ions and particles collide due to Brownian motion, thereby charging the particles. Excess ions are removed in the downstream ion trap, before the particles are collected in a Faraday cup electrometer to measure the total particle-induced current. The number of elementary charges carried by the particles depends on the particle diameter d_p and scales with ${d_p}^{1.13}$ [15, 16]. It was assumed that at least for particles >20 nm, the LDSA follows the same particle size dependence [13, 14], so that a simple calibration factor is sufficient to obtain the LDSA concentration from the measured current. The LDSA of particles below 20 nm would be overestimated by the measurement of the current. The ion trap voltage can therefore be adjusted to not only remove ions but also certain amounts of highly mobile small particles in order to adjust the instrument's response to the required one for alveolar or tracheobronchial LDSA concentration for sub-20 nm particles. It was later shown that this measurement principle is only capable of measuring the LDSA concentration accurately up to 400 nm. The LDSA concentration of larger particles

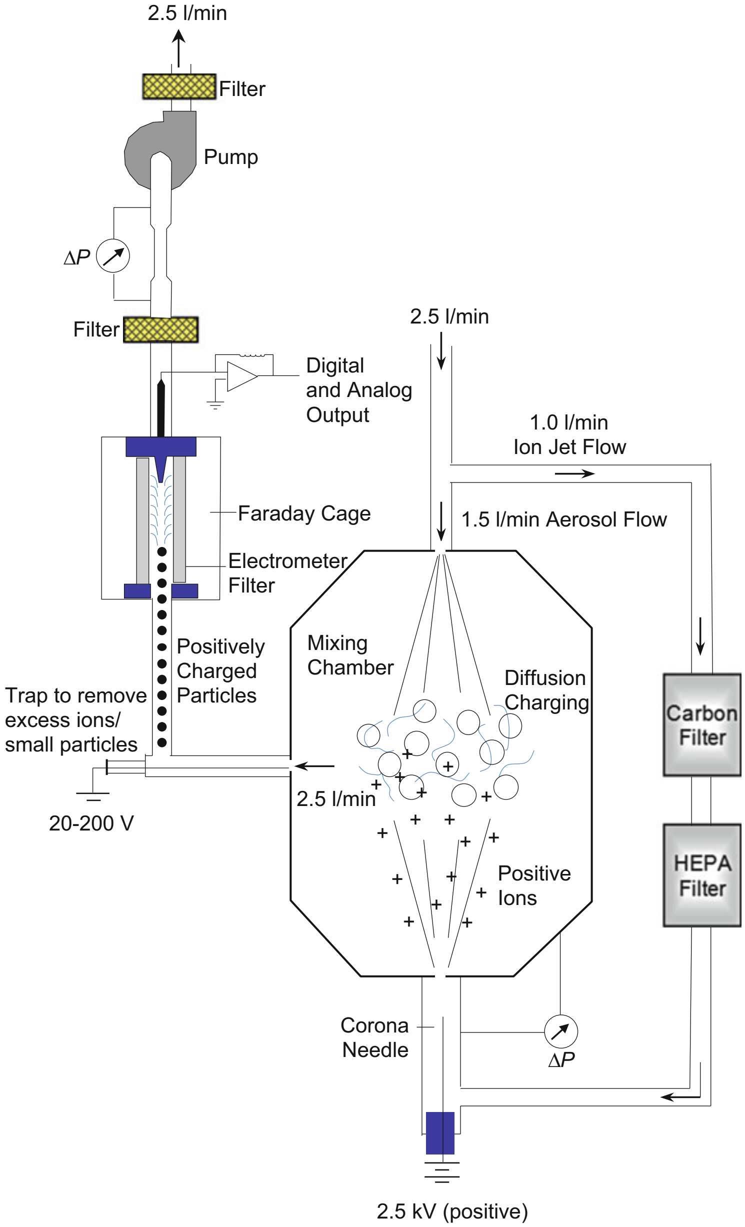


Fig. 3 Schematic of the Nanoparticle Surface Area Monitor (NSAM, TSI model 3550, image courtesy of TSI Inc.)

are drastically underestimated [17]. A corresponding new pre-separator with 450 nm cutoff and low pressure drop has been developed [18] but as of now has not yet been commercialized.

Measurement of Particle Mass Concentration

The tapered element oscillating microbalance (TEOM, Thermo Scientific) is an instrument that was designed to measure ambient particle mass concentrations. TEOM uses a filter, mounted on the tip of a hollow, tapered glass tube, which is clamped on the lower and free to vibrate on the upper end [19]. Two magnets are mounted on the sides of the glass tube near the upper end. An alternating magnetic field is applied, causing the upper end of the glass tube with the filter to vibrate at a frequency around 250 Hz. The excitation energy is constant, resulting in a constant vibration frequency as long as the mass of the system remains constant. The aerosol is drawn through the filter and the glass tube at an adjustable flow rate between 1 and 3 L/min. The particles deposit on the filter, thereby increasing its mass, causing the vibration frequency to decrease. The mass increase of the filter and hence the airborne particle mass concentration are determined from the frequency gradient. In principle, there is no upper or lower particle size limit for this method, but a minimum mass concentration needs to be available. As a rule of thumb, mass concentrations below approximately 5 $\mu g/m^3$ (equivalent to approximately 10,000 $1/cm^3$ of 100 nm particles with unit density) are no longer measurable. The particle size range can be limited at the upper end by the use of an impactor. Impactors with cutoff sizes of 10, 2.5, and 1 μm are available from the manufacturer, but none in the nano-range.

Measurement of Particle Size Distribution by Electrical Mobility Analysis

Electrical mobility analysis is the most common measurement method for the determination of number size distributions of submicron particles down to the nanometer range. The most accurate electrical mobility analyzer is the so-called scanning mobility particle sizer (SMPS) [20], which is an advancement of the earlier differential mobility particle sizer (DMPS) [21, 22]. SMPS and DMPS consist of four major components (see Fig. 4), i.e., an impactor to remove all particles that are too large, a neutralizer to charge the particles to a known bipolar charge distribution [23, 24], a differential mobility analyzer (DMA) [25] to classify the particles, and a condensation particle counter (CPC) to determine the concentration of the classified particles. The main advantage of SMPS over DMPS is its higher time resolution. While a DMPS takes about 15 min to complete the measurement of a size distribution, the SMPS only requires a few minutes. Since DMPS systems are no longer commercially available, only SMPS will be covered in the following. The SMPS is currently considered the state of the art and most accurate

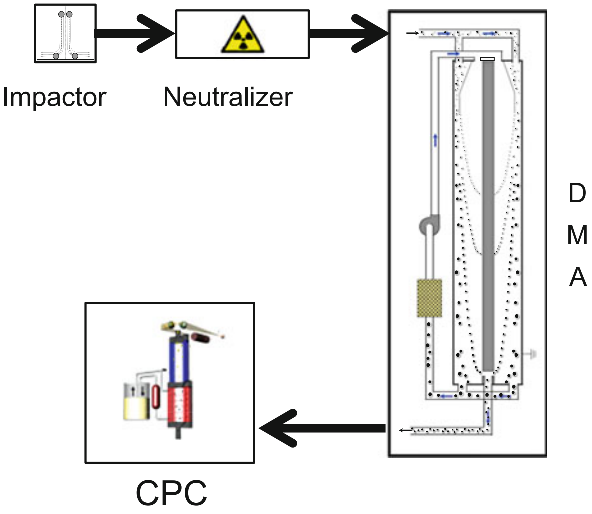


Fig. 4 Schematic of an SMPS and DMPS (CPC, image courtesy of Palas GmbH; DMA, image courtesy of TSI Inc.)

means for measuring number size distributions of airborne submicron particles [26, 27].

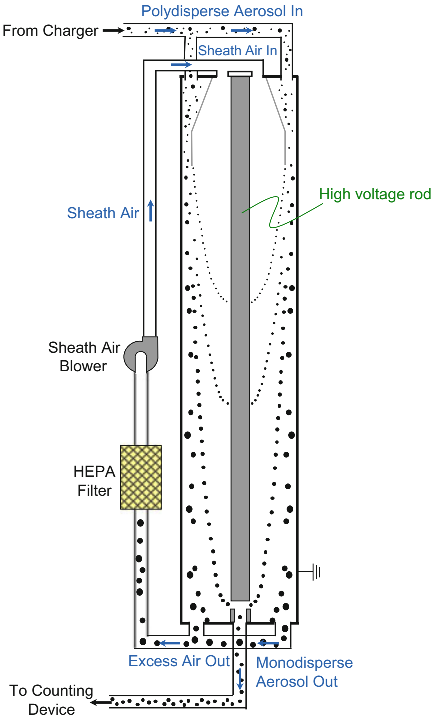
The DMA (see Fig. 5) is the key component of an SMPS. It classifies particles according to their electrical mobility Z_p:

$$Z_p = \frac{n \cdot e \cdot C_c(d_m)}{3\pi \cdot \eta \cdot d_m}. \tag{1}$$

In Eq. (1), d_m is the electrical mobility particle diameter, n is the number of particle-borne elementary charges e (1.602×10^{-19} As), C_c is the Cunningham slip correction factor [28, 29], and η is the gas viscosity. The electrical mobility diameter describes that the particle under consideration behaves in the electric field of the DMA like a spherical particle of this diameter. If the particle is spherical, the electrical mobility diameter equals the geometric sphere diameter, whereas in case of nonspherical particles, it is the diameter of an equivalent sphere.

The DMA is essentially a coaxial capacitor with an inner and an outer electrode. The charged test aerosol enters the DMA through an annular slit near the outer electrode and is separated from the inner electrode by a particle-free sheath flow. Typical aerosol flow rates are between 0.1 and 1.0 L/min with the sheath flow rate commonly by a factor of ten higher. At the bottom of the DMA, two flows are withdrawn, a monodisperse aerosol flow through a thin slit in the inner electrode and the remaining excess flow through the annular ring between inner and outer electrode. Usually the flow rate of the monodisperse aerosol flow equals the flow rate of the incoming polydisperse aerosol and the excess air flow is recycled as the sheath flow. If no voltage is applied between the inner and the outer electrode, the particles move along the outer electrode and no particles reach the monodisperse aerosol flow. If a voltage is applied, particles of one polarity (depending on

Fig. 5 Schematic of a differential mobility analyzer (DMA, image courtesy of TSI Inc.)



direction of the electric field) migrate toward the inner electrode at a velocity v_p, defined by the electrical mobility Z_p (see Eq. (1)) and the electric field strength E:

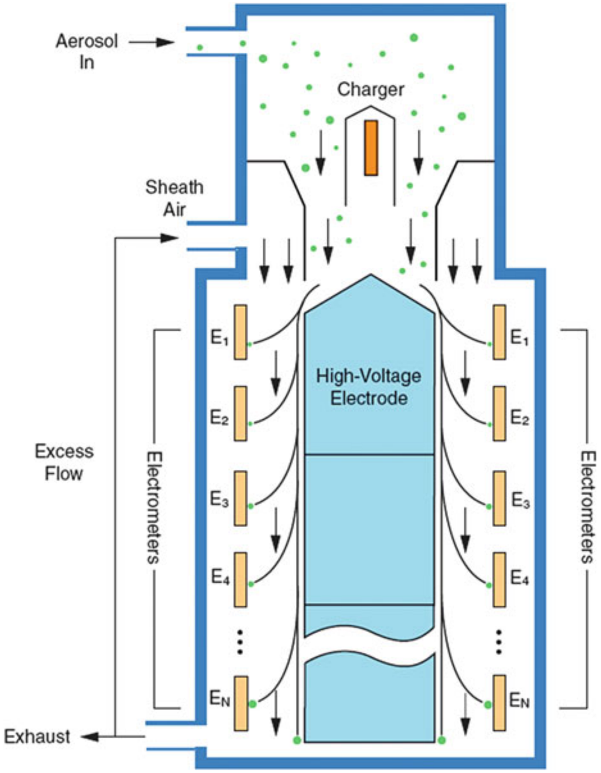
$$v_p = Z_p \cdot E. \tag{2}$$

For a given DMA voltage and thus electric field strength, only particles of a certain electrical mobility reach the slit for the monodisperse aerosol and are carried away with this flow. Particles with higher electrical mobility, i.e., smaller and/or higher charged particles, hit the inner electrode at a higher location, while particles with lower mobility are carried away with the excess flow. By changing the DMA voltage, the full range of electrical mobility can be scanned. In the SMPS, the voltage is continuously ramped, whereas in the DMPS it is increased in steps. All manufacturers offer DMAs with different column lengths to cover different particle size ranges, typically a long DMA [24, 30] to cover sizes between approximately 10 nm and 1,000 nm and a nano-DMA [31, 32] to extend the size range down to 2.5 nm or even below. The concentration of the mobility-classified particles is measured by a CPC downstream of the DMA. From Eq. (1), it is apparent that different combinations of particle size and number of elementary charges result in equal electrical mobility. Thus, the classified aerosol exhibits a multimodal size distribution with discrete peaks, each one representing a certain number of particle-borne elementary charges and the corresponding particle size. The primary output of the SMPS is hence the number concentration of classified particles as a function of their electrical mobility. A complex data deconvolution routine [33] is used to obtain the number size distribution from the mobility distribution, taking into account the charge distribution the particles acquire in the neutralizer [23, 24], the diffusion losses of particles in the system and the DMA [34], the DMA transfer function [35], and the counting efficiency of the CPC [36, 37]. Due to its statistical data evaluation routine, the CPC needs to count a certain number of classified particles downstream of the DMA in each size channel. As a rule of thumb, size distributions with number concentrations below 1,000 $1/\mathrm{cm}^3$ should be treated critically. The size distributions are delivered with resolutions up to 64 size channels per size decade. To make number size distributions measured with different size resolutions comparable, the concentration data usually gets normalized with respect to the size channel width, i.e., commonly as $dN/d\log(d_p)$. SMPS instruments are available from several manufacturers including (in alphabetical order) Grimm Aerosol (Ainring, Germany), HCT (Korea), Palas (Karlsruhe, Germany), and TSI Inc. (Shoreview, MN, USA). For a long time, the main downside of the SMPS was its need for a radioactive neutralizer (mainly $^{85}\mathrm{Kr}$ or $^{241}\mathrm{Am}$). More recently, all SMPS manufacturers introduced soft X-ray neutralizers [38–40] as nonradioactive alternatives which require significantly lower bureaucratic efforts.

The fast mobility particle sizer (FMPS, TSI model 3091) is an alternative to the SMPS. It follows the same overall principle, i.e., electrical mobility analysis, but differs in numerous details. The main advantage of the FMPS over the SMPS is its high time resolution of 1 s. The high time resolution, however, comes at the price of reduced accuracy [26, 27] and size resolution. Figure 6 shows a schematic of the FMPS.

The aerosol is taken in at a flow rate of 10 L/min and first passes a (nonradioactive) unipolar corona charger to positively charge the particles, before it enters a coaxial classifier near the inner electrode. Inside the classifier, the aerosol flow is surrounded by a particle-free sheath flow at a flow rate of 40 L/min. A positive high voltage is applied to the inner electrode to repel the particles toward the outer electrode. The voltage is kept constant and therefore the location where the particles hit the outer electrode is a function of their electrical mobility. The outer electrode consists of an array of 22 electrode rings, electrically insulated from each other. Each electrode ring therefore represents a certain electrical mobility bandwidth and is connected to an electrometer which measures the current induced by the deposition of charged particles. A data deconvolution routine is used to determine the number size distribution from the current distribution, taking into account the charge distribution of the particles downstream of the corona charger. It is known that unipolar corona chargers have a charging efficiency which is proportional to approximately $d_p^{1.1}$ [15]. Taking into account that the Cunningham slip correction factor decreases very steeply with increasing particle size for particles smaller than around 100 nm, but gets a very weak function of the particle diameter for sizes >200 nm to eventually become constant, it is obvious from Eq. (1) that the dependence of the electrical mobility on particle size for particles larger than

Fig. 6 Schematic of the fast mobility particle sizer (FMPS, TSI model 3091, image courtesy of TSI Inc.)



>200 nm gets increasingly weak and reaches a minimum around 400 nm [41]. Although the instrument is supposed to cover a size range from 5.6 to 560 nm, the sizing accuracy for particles larger than approximately 200 nm is rather poor [26, 27, 41], whereas the overall agreement for particle sizes below 100 nm is typically acceptable.

Measurement of Particle Size Distribution by Inertial Separation

Other instruments to obtain size-resolved information on airborne particles are cascade impactors. The process of inertial particle removal is known as impaction. In an impactor, the aerosol is first accelerated in a nozzle before it is diverted by 90° around an impaction plate. While small particles follow the streamlines, larger particles with high inertia divert from the streamlines and are deposited on the impaction plate (see Fig. 7).

Whether or not a particle is deposited by impaction can be determined by means of the dimensionless Stokes number *Stk*. The Stokes number is defined as the ratio of the stopping distance of a particle and the characteristic size of the flow obstacle.

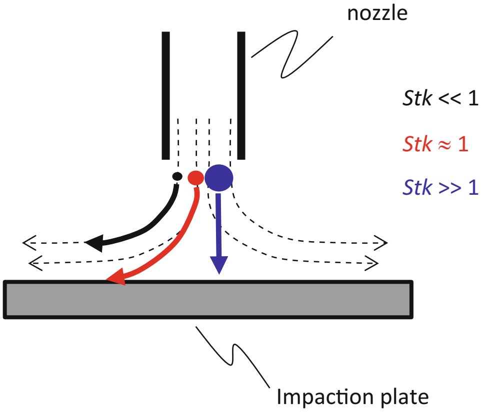


Fig. 7 Principle of an impactor

For $Stk << 1$, the particles follow the streamlines perfectly, whereas for $Stk >> 1$, the particles move straight, more or less independent of the flow direction. For an impactor with round nozzles, it is usually assumed that 50% of the particles get deposited in case of $Stk_{50} = 0.24$ [42]. The corresponding particle size d_{50}, at which 50% of the particles are deposited, is also referred to as the cutoff diameter. The cutoff diameter is a characteristic parameter of an impactor and can be determined by Eq. (3):

$$d_{50}\sqrt{C_c(d_{50})} = \left[\frac{9\pi \cdot \eta \cdot D_j^3 \cdot Stk_{50}}{4 \cdot \rho_p \cdot Q}\right]^{\frac{1}{2}}. \tag{3}$$

In Eq. (3), η is the gas viscosity, D_j is the nozzle diameter, ρ_p is the particle density, and Q is the flow rate. Since the collection efficiency depends not only on particle size but also on particle density (see Eq. (3)), the particle diameter is described as an aerodynamic equivalent diameter d_{ae}. The aerodynamic diameter describes that the (irregularly shaped) particle under consideration settles or impacts like a sphere with unit density ($\rho_0 = 1$ g/cm^3 = 1,000 kg/m^3) of this size. For a spherical water droplet, the aerodynamic diameter is the same as the droplet diameter. In case of two particles with identical sizes but with different densities, the particle with higher density has a larger aerodynamic diameter than the one with lower density:

$$d_{ae} = d_m \cdot \sqrt{\frac{\rho_p}{\rho_o}}. \tag{4}$$

As shown in Eq. (3), for a given flow rate, the cutoff size of an impactor can be varied by varying the nozzle diameter. A cascade impactor uses a multitude of sequential impaction stages with decreasing nozzle diameters, thus stage by stage decreasing the cutoff size. The particles collected on each impaction plate therefore cover the size range defined by the cutoff size of the preceding and this stage. The impaction plates may be weighed before and after particle collection to determine the mass size distribution, or they can be analyzed chemically or by electron microscopy to obtain the size-resolved chemical composition or particle morphology, respectively. Most cascade impactors sample particles in the micron size range, although some exist that can collect particles down to a few nanometers (e.g., the multi-orifice uniform deposit impactor (MOUDI) from MSP, Shoreview, MN, USA). Since the inertia of particles scales with the particle mass, i.e., the particle size to the third power, nanoscale particles only have a very low inertia. In order to be able to capture them by impaction, the opposing drag force has to be lowered by reducing the pressure.

The electrical low-pressure impactor (ELPI or ELPI+, Dekati, Tampere, Finland [43]) uses a total of 13 impaction stages and an after-filter stage to collect particles with sizes between 6 nm and 10 μm. In order to collect such small particles, the last collection stage operates at a pressure of only 100 mbar. In contrast to conventional cascade impactors, ELPI first charges the particles in a unipolar charger, and each impaction stage is connected to a sensitive electrometer to measure the current induced by the collected particles as shown in Fig. 8. With the known charge distribution downstream of the unipolar charger, the number size distribution is determined from the measured current distribution. The time resolution of ELPI is variable and can be up to 0.1 s if the particle concentration is sufficiently high for the measured currents to be well above the electrometer noise level. ELPI is

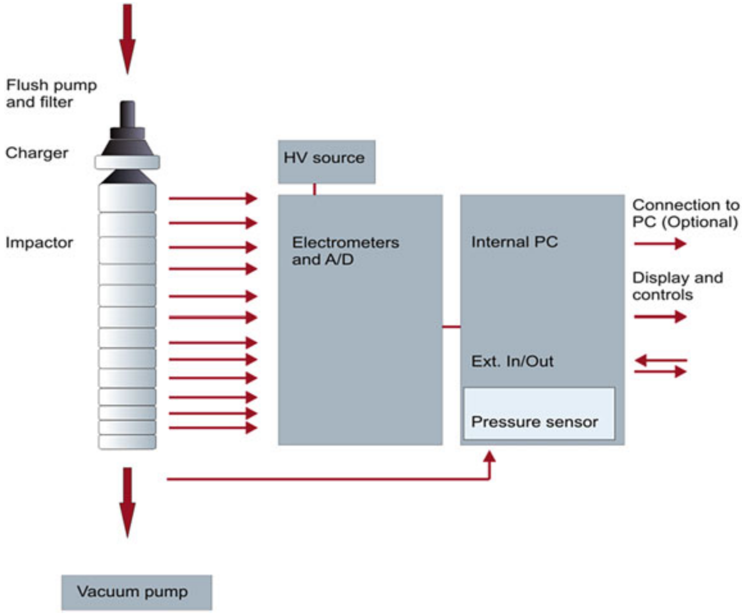


Fig. 8 Schematic of the electrical low-pressure impactor (ELPI or ELPI+, Dekati, Finland, image courtesy of Dekati)

currently the only instrument available that measures particle size distributions from a few nanometers up to 10 μm based on the same measurement principle, thus bypassing the challenge of converting size distributions based on different equivalent diameters. After sampling, the impaction plates are available for further analyses, for example, concerning the particle morphology or chemical composition.

2.1.2 Time-Integrating Instruments

Time-integrating instruments are used to collect particles over a certain time for subsequent analyses. Different collection mechanisms and substrates are used. The main collection mechanisms are filtration as well as electrostatic and thermal collection. Substrates need to be chosen to be suitable for the subsequent analysis. The only main size-resolving sampling technique is the cascade impactor, which is described in the section on the electrical low-pressure impactor above. All other time-integrating samplers do not deliver particle size-resolved samples; however, depending on the substrate and analysis, size-resolved information may be obtained, for example, through electron microcopy. In most cases, the size range of the collected particles may be limited at the upper end by the use of an appropriate upstream impactor.

Filter Sampling

Filter samplers are rather simple devices, in which the aerosol is drawn through a filter at a known flow rate to collect the particles. Depending on the planned analysis, fiber or membrane filters are used. Fiber filters are typically used to determine the average particle mass concentration by weighing the filter prior to and after sampling. The filters can subsequently also be used for chemical analyses of the collected particles, for example, by inductively coupled plasma mass spectrometry (ICP-MS) or by thermal analysis for elemental and organic carbon (EC-OC analysis) [44]. Alternatively, membrane (e.g., Nuclepore) filters can be used if the particles are to be collected on the filter surface. In this case, they can, for example, be washed off more easily. The resulting suspension can then be analyzed, for example, by electron spin resonance spectroscopy for the potency of the particles to generate reactive oxygen species (ROS) [45]. The potency of particles to generate ROS is an indicator that the particles may cause lung inflammation upon inhalation. Chen et al. [46] used membrane filters to eventually evaluate the particle size distribution of the collected agglomerates and aggregates by electron microscopy. With the help of a particle deposition model for the membrane filter, the size distribution of the particles in the airborne state is reconstructed.

Filter samplers are typically used in combination with an impactor upstream to limit the particle sizes to a maximum of 10 μm (PM_{10}), 4 μm (respirable fraction), 2.5 μm ($PM_{2.5}$), or 1 μm (PM_1).

Electrostatic Sampling

If a charged particle is exposed to an electric field, a Coulomb force makes the particle move in direction or counter direction (depending on polarity of the net particle charge) of the electric field (see Eq. (2)). In a DMA (see Fig. 5), this phenomenon is used to classify particles, but it can also be utilized to collect charged particles on a substrate in an electrostatic precipitator. The commercially available stationary ESPs collect incoming particles on a flat substrate inside a metallic cup. A schematic of an electrostatic precipitator for particle sampling is shown in Fig. 9. This concept is realized in the Grimm electrostatic precipitator (Grimm Aerosol model 5.561) and the TSI nanometer aerosol sampler (NAS, TSI model 3089). The aerosol enters the ESP through a circular inlet in the top of the housing at a flow rate between 1 and 5 L/min, flows around the inner electrode with the substrate, and is discharged through the outlet in the bottom. The outer housing of the ESP is grounded and a high positive or negative potential is applied to the inner electrode, thereby establishing an electric field between the inner and outer electrode, which drives the particles onto the surface of the substrate, where they are collected [47]. Typical substrates include semiconductor (silicon or gallium arsenide) wafers or wafer chunks, TEM grids, or glassy carbon. The spot size of the collected particles can be adjusted by adjusting the collection voltage. Semiconductor wafers have perfectly flat surfaces and are therefore well suited for scanning electron microscope (SEM) analyses. TEM grids are used for transmission electron

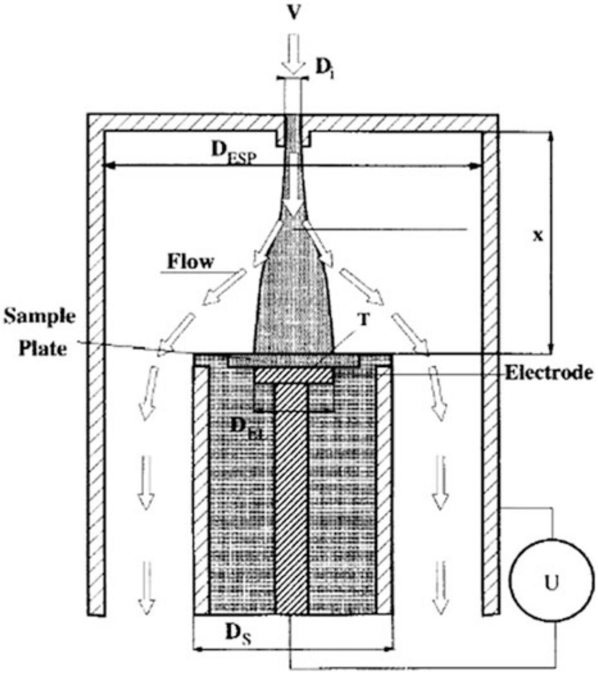


Fig. 9 Schematic of an electrostatic precipitator (from [48])

microscope (TEM) analyses. In both cases, the particles can be analyzed for their sizes and morphologies or in combination with electron dispersive X-ray (EDX) spectroscopy for their chemical composition. While TEM is able to analyze the substrates with higher resolution than SEM, the use of an SEM is easier and less cost intensive. For electron microscopic analyses, it is necessary not to overload the substrates to avoid that particles deposit on top of each other, thereby becoming indistinguishable. A wider deposition spot size is therefore preferred, which can be achieved by choosing a relatively low collection voltage. Glassy carbon substrates are used to collect particles for subsequent total X-ray fluorescence (TXRF) spectroscopy [48]. TXRF requires the particles to be collected in a small spot, which is achieved by a high collection voltage.

The commercially available stationary ESPs are designed to collect monodisperse particles downstream of a DMA (see Fig. 5). Since particles leaving a DMA are always charged, the ESPs do not contain means for particle charging. If these ESPs are used for sampling unclassified polydisperse particles, one may rely on the natural charge of airborne particles. Once airborne, particles interact with the ubiqituous air ions. Aged airborne particles are therefore usually charged according to a Boltzmann distribution, i.e., with more or less equal amounts of positive and negative charges. Only particles of one polarity would then be collected in the ESP. Alternatively, a unipolar charger can be used upstream; however, as of now, no commercial solution is available.

2.2 Portable Equipment

Portable measurement equipment is characterized by its ability to measure independent of mains power and by its smaller size compared with stationary equipment. Portable instruments are sufficiently mobile to be easily moved between different measurement locations and are therefore suitable for measurements according to tier 2 in tiered workplace exposure assessment. Portable equipment typically has a lower accuracy and lower sizing resolution than stationary equipment. The measurement methods of portable instruments are all the same or very similar to the ones described above for the stationary equipment and are therefore not repeated here. Instead, the instruments are only briefly introduced.

2.2.1 Time-Resolving Instruments

Measurement of Particle Number Concentration

Handheld condensation particle counters (handheld CPCs) are available to measure the particle number concentration of airborne particles. These handheld CPCs use isopropyl alcohol (IPA) as working fluid and are battery operable. During operation, the handheld CPCs have to be maintained in a horizontal orientation to avoid flooding of the optics with IPA. Depending on model, their lower size limit is 10 nm (TSI CPC model 3077, Kanomax model 3800) or 20 nm (TSI P-Trak), respectively. Their concentration range is nominally limited to 100,000 1/cm^3 in case of TSI model 3077 and Kanomax model 3800 and 500,000 1/cm^3 in case of TSI P-Trak. Above this limit, coincidence errors may occur, resulting in too low concentrations being reported by the CPCs. However, no alarm is given in this case. The TSI model 3077 was shown to be accurate to within ±5% [49] as long as the instrument is well calibrated and the concentrations are within the instrument's specified concentration range. More recently, it was found that the TSI P-Trak seems to show coincidence errors already for concentration higher than 100,000 1/cm^3 [50], despite the much higher specified concentration limit.

Other instruments that may be considered portable number concentration measuring instruments are based on diffusion charging, such as the DiSCmini (Testo GmbH, Titisee-Neustadt, Germany [51]) or NanoTracer (Oxility, Eindhoven, the Netherlands [52, 53]). These instruments are, however, small enough that they can also be used as personal measuring instruments and are therefore described below in the section on personal measurement equipment.

Measurement of Lung-Deposited Surface Area Concentration

The Nanoparticle Surface Area Monitor (NSAM, TSI model 3550; see above) has been downsized and differently packaged to make the instrument smaller, portable, and battery operable. This instrument has been commercialized by TSI as Aerotrak 9000. It is essentially the same instrument as NSAM and shows a similar accuracy [17] and comparability.

Other instruments that can be considered as portable devices for the measurement of LDSA concentrations are DiSCmini and NanoTracer and are described below under personal measurement equipment.

Measurement of Particle Size Distribution

Portable instruments for the measurement of submicron particle number size distributions have rather recently entered the market. They are all based on electrical mobility analysis and are in principle very similar to the SMPS described above. All these instruments are able to operate on battery power for several hours and independent of an external computer.

The portable aerosol mobility spectrometer (PAMS, Kanomax) follows the same but miniaturized setup as the SMPS (see Fig. 4) with the main exception that the neutralizer is a bipolar corona charger which provides a similar charge distribution like a radioactive or soft X-ray charger. The following DMA is of the radial type [54], i.e., it consists of two parallel circular electrodes. The aerosol and the sheath flow enter the space between the electrodes from outside and are discharged through central holes in the top and bottom electrode, respectively. The monodisperse aerosol is guided to a CPC, which is basically the Kanomax handheld CPC, incorporated into the system. PAMS can be operated in two flow rate modes. With an aerosol flow rate of 0.2 L/min, it measures the size distribution in a size range from 14.5 to 863 nm in $\geq$42 s and with 0.4 L/min in a range from 10 to 433 nm in $\geq$81 s.

The TSI NanoScan (model 3910) [55] follows essentially the same setup as PAMS but uses a unipolar corona charger to replace the radioactive neutralizer. NanoScan determines the number size distribution of airborne particles, nominally in a size range from 10 to 420 nm with a time resolution of 60 s. The unipolar charger has a similar particle charging characteristic like the unipolar charger used in the FMPS (see above) and therefore gives rise to the same challenges in the electrical mobility analysis of particles larger than approximately 200 nm, due to the increasingly weak dependence of the electrical mobility on particle size. This phenomenon has been shown experimentally [56]. It was found that the sizes of a polydisperse DEHS aerosol with a 200 nm modal diameter were significantly underestimated by NanoScan. The number concentration of a NaCl aerosol with 10 nm modal diameter was drastically underestimated by NanoScan in the same study. Measurements with other aerosols with modal diameters between 10 and 200 nm delivered satisfying results. Stabile et al. [57] found acceptable agreement of NanoScan size distributions with those measured by SMPS, but they reported significant deviations for agglomerated particles.

The nano-ID NPS500 (Naneum, Canterbury, UK) determines size distributions in a size range from 5 to 500 nm with a time resolution of $\geq$30 s. It uses a patented unipolar corona charger and a planar DMA [58]. The charger limits the number of multiple charges on the particles which simplifies the data deconvolution. The design of the electrical mobility classifier is not disclosed. The CPC operates on a patented organic working fluid, which allows for a very long operation of up to months without the need for a refill.

Grimm Aerosol (Ainring, Germany) follows a different concept for their portable particle sizer. In the mini-wide range aerosol spectrometer (mini-WRAS, model 1.371), they combine an optical spectrometer to optically measure the number size distribution in a particle size range from 200 nm to 35 μm with a simplified electrical mobility analyzer to extend the measurement range down to 10 nm. Inside the electrical mobility classification part, the incoming aerosol is charged in a unipolar corona charger, followed by a concentric electrical mobility classifier. Unlike in a DMA, the classifier operates without sheath flow. Instead, the current from all charged particles leaving the classifier is measured with a downstream electrometer. By increasing the voltage in the classifier, an increasing amount of particles is removed from the aerosol and deposited inside the classifier. Due to the size dependence of the electrical mobility, the current gradient as function of classifier voltage can be tracked back to the particle number size distribution.

The eventual size distribution is delivered with a total size resolution of 40 size channels, ten from the electrical and 30 from the optical measurement.

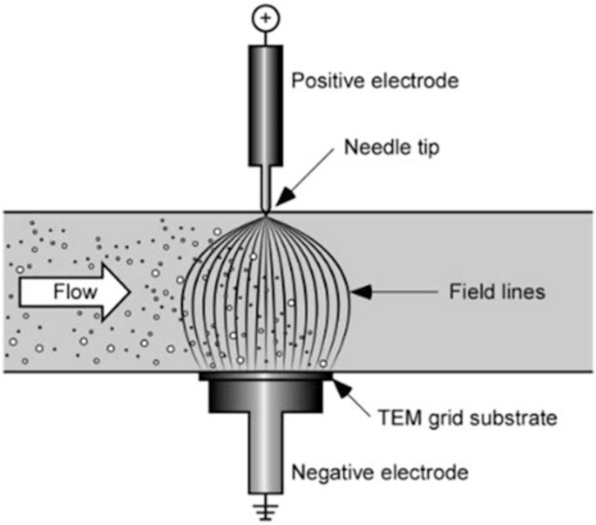


Fig. 10 Schematic of ESPnano model 100; image from [59]

2.2.2 Time-Integrating Instruments

A novel, commercial handheld ESP is available from ESPnano (model 100, ESPnano, Spokane, WA, USA [59]). The sampler is small and battery operated and collects airborne particles onto TEM grids. A schematic of the ESP is shown in Fig. 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 a certain, for example, critical substance.

The ESPnano model 100 uses a unipolar corona charger to generate ions near a tip electrode. When a positive high voltage is applied to the tip, a corona is formed that ionizes 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 is performed.

2.3 Personal Equipment

Personal measurement equipment is characterized, similar to portable measurement equipment, by its ability to measure independent of mains power. Additionally, the devices should be sufficiently small, lightweight, and robust so that they could be worn by a worker over an 8-h shift and would not interfere or affect with any of the activities carried out by the worker. They should also be easy to use for nonspecialist personnel. Only very recently, nanospecific personal samplers and monitors have become available that are capable of measuring different metrics, i.e., number concentration and mean particle size, LDSA concentration, mass concentration, etc., in the breathing zone of a human. As most of them are available only as prototypes, only the commercially available ones will be described and some additional examples of prototypes will be mentioned. An overview of the working principles of the personal monitors is given in Fig. 11.

2.3.1 Time-Resolving Instruments

Measurement of Number Concentration, Lung-Deposited Surface Area Concentration, and Mean Particle Size

The DiSCmini (Testo GmbH, Titisee-Neustadt, Germany), as well as its original prototype, the miniDiSC (University of Applied Sciences and Arts Northwestern Switzerland, Windisch, Switzerland), is a portable, battery-operated instrument that determines the alveolar LDSA concentration, number concentration, and mean particle size with a time resolution of 1 s [51]. The instrument draws the test aerosol at a flow rate of 1 L/min through an optional impactor, where particles larger than 700 nm are removed. The remaining particles pass through a positive unipolar diffusion charger, acquiring an average charge that is approximately proportional to the particle diameter. Then the charged particles pass through an ion trap where the excess ions are removed and finally a dual-stage particle deposition system. The first stage consists of a stack of stainless steel grids where preferentially small particles are deposited due to Brownian diffusion. The second stage consists of a high efficiency filter, where the remaining particles are collected. Both stages are connected to Faraday cup electrometers that continuously measure the current induced by the deposited particles (see Fig. 11 for the schematic of the working principle). With these two independent measurements, the mean particle size and the total particle number concentration can be determined from the ratio and the sum of the currents by assuming a lognormal particle size distribution with a geometric standard deviation of $\sigma_g = 1.9$. In addition, the total current, i.e., the sum of the currents from both stages, is proportional to the lung-deposited surface area concentration, as from approximately 20–400 nm the LDSA and the charging efficiency of the DiSCmini charger follow nearly the same size dependence and can therefore be determined by applying a simple calibration factor.

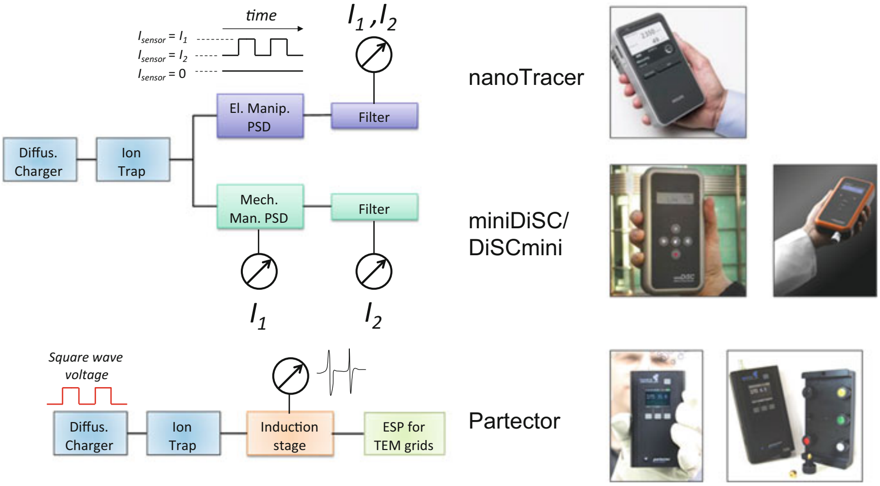


Fig. 11 Schematic of the working principle of the diffusion charger-based monitors: NanoTracer (*top*), DiSCmini/miniDiSC (*middle*), and Partector (*bottom*)

Another portable instrument based on the unipolar diffusion charging of particles is the NanoTracer (discontinued by Philips Aerasense, Eindhoven, the Netherlands, recently licensed by Oxility, Eindhoven, the Netherlands). The instrument draws the aerosol at a flow rate between 0.3 and 0.4 L/min, and after charging the particles in a unipolar corona charger, these pass in between two parallel electrodes, to which a square wave voltage is applied [52]. As long as the voltage is zero, no particles are removed and a very sensitive electrometer downstream of the electrode system measures the charge of all particles. When a certain voltage is applied to the electrodes, a fraction of small particles with high electrical mobility deposits on the electrodes and subsequently a lower current is measured by the electrometer. The alveolar LDSA concentration is determined from the current measured during zero-voltage phases. The number concentration and mean particle size are derived from the two different currents measured during high and zero voltage applied to the precipitator, respectively. The NanoTracer can operate in two different modes: fast mode, when, by assuming a mean particle size equal to 50 nm, the particle number concentration is being measured in real time (3 s), and advance mode (minimum time resolution 16 s), when both particle number concentration and averaged particle size are being determined. Only newer versions of the NanoReporter software (e.g., 1.1.0.96) permit the evaluation of NanoTracer data for LDSA concentration [53].

The DiSCmini and the NanoTracer are not small enough to directly sample in the breathing zone of an individual, but they can be worn on a belt and take aerosol samples from the breathing zone through a flexible tube.

Measurement of Lung-Deposited Surface Area Concentration

Partector is a small battery-operated personal monitor that determines the LDSA concentration with a time resolution of 1 s and is small enough to directly sample in the breathing zone of a worker. The aerosol is drawn in at 0.5 L/min, then passes a unipolar diffusion charger, followed by an ion trap and an induction stage, where the particle charge is detected with a Faraday cup electrometer [60]. When there is a temporal charge gradient in the induction stage, a current spike is induced with a magnitude proportional to the charge gradient. In order to trigger these charge gradients, the unipolar charger is operated with a square wave voltage, i.e., it gets intermittedly switched on and off with a frequency of 10 Hz. In consequence, a periodic signal is measured at the electrometer, the amplitude of which is determined in the instrument. The amplitude of this signal is proportional to the charge carried by the aerosol pulses and can therefore be calibrated to correspond to the LDSA concentration in the alveolar region of the lung of a reference worker, which is what the instrument reports.

The recent enhancement of the personal monitor, the Partector TEM sampler, combines the Partector with an electrostatic precipitator that deposits particles on standard TEM grids. Because the particle concentration is measured online, the sampler automatically determines the optimal probe sampling time and stops sampling when a sensible coverage of the grid is reached (~1% of the area covered with particles).

A study conducted on the accuracy and comparability of these diffusion-charging electrical aerosol monitors showed that as long as the measured particle sizes are between 20 and 400 nm, the LDSA concentrations reported by the instruments can be measured with an accuracy of ±30%. The LDSA concentrations of particles smaller than 20 nm are overestimated, whereas the LDSA concentrations of particle >400 nm are underestimated [17].

2.3.2 Time-Integrating Instruments

Thermophoretic Sampling

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 [61]. 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, transfering more net momentum per collision to the particle than do molecules on the colder side, causing a thermophoretic force. The particles will move in the direction of decreasing temperature and will eventually deposit onto the colder side of the flow channel which includes the TEM grid.

Fig. 12 The thermal precipitation sampler (TPS): the overall device including the removable sample cartridge (*left*). *Right*: view of the TPS region containing the hot plate (**a**), TEM grid holder (**b**), and cold plate (**c**) [61]

The TPS samples aerosol at a flow rate between 1 and 10 mL/min and utilizes 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 Fig. 12). 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 [62]:

$$N(d) = \left[\frac{x(d)A}{QtS}\right]\left[\frac{F(d)}{Pt(d)\eta(d)}\right]. \tag{5}$$

In Eq. (5), $x(d)$ is the number of particles with size d counted in a microscope field with area S and the total area of the substrate is A; $F(d)$ is a normalization factor that adjusts for known and unknown factors, e.g., any differences in the particle deposit between the field examined and the entire collection substrate; $Pt(d)$ is the fractional penetration of the particles through the sampler inlet; $\eta(d)$ is the fractional collection efficiency for these particles onto the sampler substrate; Q is the flow through the sampler; and t is the sampling time.

Also the first prototypes of another thermal precipitator, designed as a personal sampler for nanomaterials, have been built [63, 64].The TP samples thermophoretically particles onto silicon substrates that can be used for consecutive SEM/EDX analysis. The sampler has been evaluated and validated up to a size of 300 nm using monodisperse polystyrene latex (PSL) particles as well as soot particles.

Sampling on Different Filtration Media

The NanoBadge (NanoInspect, Alcen Group, France, and French Alternative Energies and Atomic Energy Commission) is a lightweight battery-operated portable device which collects airborne particles in the breathing zone of the worker (Fig. 13).

Fig. 13 The NanoBadge; the white cassette on the top of the device is equipped with a sealed track-etched membrane to collect airborne particles; a single on-off switch makes the device robust and very simple to use

The sampler is connected to a cassette, whose filter is analyzed offline by X-ray fluorescence spectroscopy (XRF), providing a cumulative mass-based quantification of the chemical elements present on the filters. Track-etched membranes are used to collect particles for subsequent analysis of particle size (SEM), elemental composition, and concentration (XRF). The sampler can be equipped with a pre-separator with a cutoff diameter of 4 μm (respirable fraction) to remove coarse particles. The NanoBadge 2013 version is operated with a flowrate of 0.6 L/min while the 2015 version is operated at 1 L/min. For both versions, the flow rate is kept in the range of ±5% over more than 10 h.

The measurement of the engineered nanoparticles' 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 nondestructive analytical technique, meaning that the same sample can be characterized further with other techniques such as scanning electron microscopy (SEM). After sampling, the cassettes are extracted from the NanoBadge and sent directly to the service provider (NanoInspect) for analysis and subsequent data restitution (i.e., elemental mass concentration in the breathing zone averaged over the total sampling time).

The sampler has been evaluated and validated up to a size of 200 nm using ZnO and TiO_2 particles. 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 and consequently 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 [65].

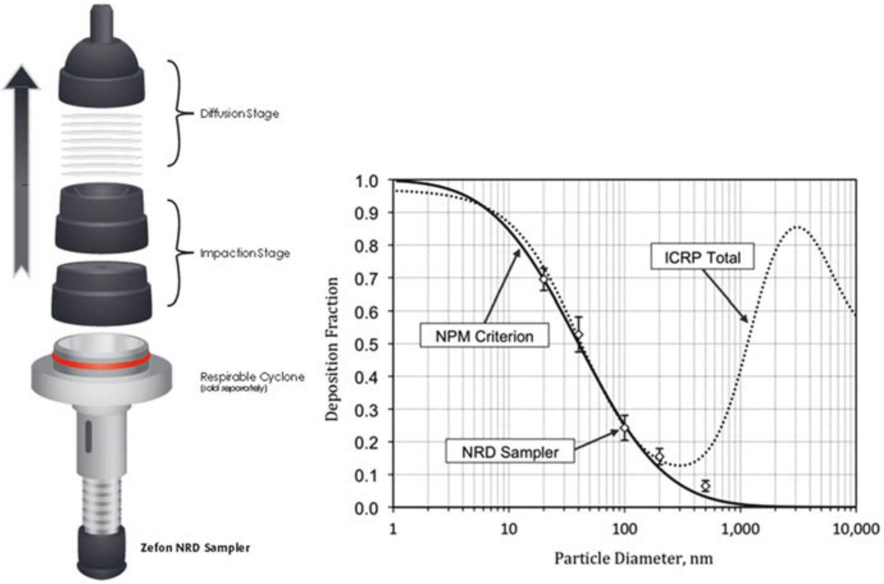


Fig. 14 Schematic of the NRD (*left*); NPM sampling criterion, ICRP total respiratory deposition, and effective deposition on the diffusion stage of the NRD sampler (*right*) [66]

The personal nanoparticle respiratory deposition (NRD, Zefon International, Ocala, FL, USA) [66] 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 submicrometer particles, that when inhaled can deposit anywhere in the respiratory tract (see Fig. 14).

The sampler operates at 2.5 L/min and consists of a respirable aluminum cyclone used to eliminate particles larger than 10 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 characterized either by chemical analysis or by scanning electron microscopy to determine the size, number, and chemical composition of the collected particles.

Other examples of samplers designed for the evaluation of the personal exposure to nanoparticles, available only in the form of prototypes, are the $PM_{0.1}$ personal sampler [67] and the personal nanoparticle sampler (PENS) [68].

The $PM_{0.1}$ personal sampler consists of a commercially available two-stage precut impactor used to remove particles in the micron size range ($PM_{1.4}$-TSP), followed by a precut 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, maximizing 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 nanpoarticles 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 d_{pa50} 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. The performance of the sampler was evaluated in three metalworking plants during a day shift of 6–8 h and showed good accuracy with respect to the reference SKC respirable dust aluminum cyclone, regardless of the particle type [69].

References

1. European Commission (2015) Definition of a nanomaterial. http://ec.europa.eu/environment/chemicals/nanotech/faq/definition_en.htm. Accessed 20 Apr 2015
2. Johnston HJ, Hutchinson G, Christensen FM, Peters S, Hankin S, Stone V (2010) A review of the in vivo and in vitro toxicity of silver and gold particulates: Particle attributes and biological mechanisms responsible for the observed toxicity. Crit Rev Toxicol 40:328–346
3. Oberdörster G (2000) Toxicology of ultrafine particles: in vivo studies. Phil Trans R Soc A 358:2719–2740
4. Xia T, Kovochich M, Brant J, Hotze M, Sempf J, Oberley T, Sioutas C, Yeh JI, Wiesner MR, Nel AE (2006) Comparison of the abilities of ambient and manufactured nanoparticles to induce cellular toxicity according to the oxidative stress paradigm. Nano Lett 6:1794–1807
5. Driscoll KE (1996) Role of inflammation in the development of rat lung tumors in response to chronic particle exposure. Inhal Toxicol 8(Suppl.):139–153
6. Bruch J, Landsiedel R, Ma-Hock L, Pauluhn J, Ragot J, Wiemann M (2009) In vivo test systems, NanoCare – Health related aspects of nanomaterials, final scientific report; Chap 4.4, pp 48–67. http://nanopartikel.info/files/projekte/NanoCare/NanoCare_Final_Report.pdf. Accessed 30 Apr 2015
7. Poland CA, Duffin R, Kinloch I, Maynard A, Wallace WAH, Seaton A, Stone V, Brown S, MacNee W, Donaldson K (2008) Carbon nanotubes introduced into the abdominal cavity of mice show asbestos-like pathogenicity in a pilot study. Nat Nanotechnol 3:423–428
8. Standard EN1540:2011 (2012) Workplace exposure. Terminology. ISBN 978-0-580-70841-1
9. McMurry P (2000) The history of condensation nucleus counters. Aerosol Sci Technol 33:297–322

10. Keller A, Tritscher T, Burtscher H (2013) Performance of water-based CPC 3788 for particles from a propane-flame soot-generator operated with rich fuel/air mixtures. J Aerosol Sci 60:67–72
11. Vincent J (2005) Health-related aerosol measurement: a review of existing sampling criteria and proposals for new ones. J Environ Monit 7:1037–1053
12. International Commission for Radiological Protection (ICRP) (1994): Publication 66: Human respiratory tract model for radiological protection. Ann ICRP 24:1–3
13. Fissan H, Neumann S, Trampe A, Pui DYH, Shin WG (2007) Rationale and principle of an instrument measuring lung deposited nanoparticle surface area. J Nanopart Res 9:53–59
14. Shin W, Pui DYH, Fissan H, Neumann S, Trampe A (2007) Calibration and numerical simulation of nanoparticle surface area monitor (TSI model 3550 NSAM). J Nanopart Res 9:61–69
15. Jung H, Kittelson DB (2005) Characterization of aerosol surface instruments in transition regime. Aerosol Sci Technol 39:902–911
16. Kaminski H, Kuhlbusch TAJ, Fissan H, Ravi L, Horn HG, Han HS, Caldow R, Asbach C (2012) Mathematical description of experimentally determined charge distributions of a unipolar diffusion charger. Aerosol Sci Technol 46:708–716
17. Todea AM, Beckmann S, Kaminski H, Asbach C (2015) Accuracy of eletrical aerosol sensors measuring lung deposited surface area concentrations. J Aerosol Sci. in press, http://dx.doi.org/10.1016/j.jaerosci.2015.07.003
18. Asbach C, Fissan H, Kaminski H, Kuhlbusch TAJ, Pui DYH, Horn HG, Hase T (2011) A low pressure drop preseparator for eliminiation of particles larger than 450 nm. Aerosol Air Qual Res 11:487–496
19. Patashnick H, Rupprecht EG (1991) Continuous PM-10 measurements using the tapered element oscillating microbalance. J Air Waste Manag Assoc 41:1079–1083
20. Wang SC, Flagan RC (1990) Scanning electrical mobility spectrometer. Aerosol Sci Technol 13:230–240
21. Fissan HJ, Helsper C, Thielen HJ (1983) Determination of particle size distributions by means of an electrostatic classifier. J Aerosol Sci 14:354–357
22. Kousaka Y, Okuyama K, Adachi M (1985) Determination of particle size distribution of ultrafine aerosols using a differential mobility analyzer. Aerosol Sci Technol 4:209–235
23. Fuchs NA (1963) On the stationary charge distribution on aerosol particles in bipolar ionic atmosphere. Geofisica pura e applicata 56:185–193
24. Wiedensohler A (1988) An approximation of the bipolar charge distribution for particles in the submicron size range. J Aerosol Sci 19:387–389
25. Liu BYH, Pui DYH (1974) A submicron aerosol standard and the primary absolute calibration of the condensation nuclei counter. J Colloid Interface Sci 47:155–171
26. Asbach C, Kaminski H, Fissan H, Monz C, Dahmann D, Mülhopt S, Paur HR, Kiesling HJ, Herrmann F, Voetz M, Kuhlbusch TAJ (2009) Comparison of four mobility particle sizers with different time resolution for stationary exposure measurements. J Nanopart Res 11:1593–1609
27. Kaminski H, Kuhlbusch TAJ, Rath S, Götz U, Sprenger M, Wels D, Polloczek J, Bachmann V, Kiesling H-J, Dziurowitz N, Schwiegelshohn A, Monz C, Dahmann D, Asbach C (2013) Comparability of mobility particle sizers and diffusion chargers. J Aerosol Sci 57:156–178
28. Cunningham, E. (1910) On the velocity of steady fall of spherical particles through fluid medium. Proc R Soc Ser A 83:357–365
29. Kim JH, Mulholland GW, Kuckuck SR, Pui DYH (2005) Slip correction measurements of certified PSL nanoparticles using a nanometer differential mobility analyzer (Nano-DMA) for Knudsen Number from 0.5 to 83. J Res Natl Inst Stand Technol 110:31–54
30. Winkelmayr W, Reischl GP, Lindner AO, Berner A (1991) A new electromobility spectrometer for the measurement of aerosol size distributions in the size range from 1 to 1000 nm. J Aerosol Sci 22:289–296
31. Chen DR, Oui DYH, Hummes D, Fissan H, Quant FR, Sem GJ (1998) Design and evaluation of a nanometer aerosol differential mobility analyzer (Nano-DMA). J Aerosol Sci 29:497–509

32. Reischl GP, Mäkelä JM, Necid J (1997) Performance of Vienna type differential mobility analyzer at 1.2–20 nanometer. Aerosol Sci Technol 27:651–672
33. Hoppel WA (1978) Determination of the aerosol size distribution from the mobility distribution of the charged fraction of aerosols. J Aerosol Sci 9:41–54
34. Reineking A, Porstendörfer J (1986) Measurements of particle loss functions in a differential mobility analyzer (TSI, model 3071) for different flow rates. Aerosol Sci Technol 5:483–486
35. Stolzenburg MR (1988) An ultrafine aerosol size distribution measuring system, Ph.D. Thesis at the University of Minnesota
36. Wiedensohler A, Orsini D, Covert DS, Coffmann D, Cantrell W, Havlicek M, Brechtel FJ, Russell LM, Weber RJ, Gras J, Hudson JG, Litchy M (1997) Intercomparison study of the size-dependent counting efficiency of 26 condensation particle counters. Aerosol Sci Technol 27:224–242
37. Hermann H, Wehner B, Bischof O, Han H-S, Krinke T, Liu W, Zerrath A, Wiedensohler A (2007) Particle counting efficiencies of new TSI condensation particle counters. J Aerosol Sci 38:674–682
38. Shimada M, Han BW, Okuyama K, Otani Y (2002) Bipolar charging of aerosol nanoparticles by a soft X-ray photoionizer. J Chem Eng Jpn 35:786–793
39. Han BW, Shimada M, Okuyama K, Choi M (2003) Classification of monodisperse aerosol particles using an adjustable soft X-ray charger. Powder Technol 135:336–344
40. Lee HM, Kim CS, Shimada M, Okuyama K (2005) Bipolar diffusion charging for aerosol nanoparticle measurement using a soft X-ray charger. J Aerosol Sci 36:813–829
41. Levin M, Gudmundsson A, Pagels JH, Fierz M, Molhave K, Jensen KA, Koponen IK (2015) Limitations in the use of unipolar charging for electrical mobility sizing instruments. Aerosol Sci Technol 49:556–565
42. Hinds WC (1999) Aerosol technology: properties, behavior, and measurements of airborne particles, 2nd edn. Wiley, New York
43. Keskinen J, Pietarinen K, Lehtimäki M (1992) Electrical low pressure impactor. J Aerosol Sci 23:353–360
44. Watson JG, Chow JC, Chen LWA (2005) Summary of organic and elemental carbon/black carbon analysis methods and intercomparison. Aerosol Air Qual Res 5:65–102
45. Janssen NAH, Yang A, Strak M, Steenhof M, Hellack B, Gerlots-Nijland ME, Kuhlbusch T, Kelly F, Harrison R, Brunekreef B, Hoek G, Cassee F (2014) Oxidative potential of particulate matter collected at sites with different source characteristics. Sci Total Environ 472:572–581
46. Chen S-C, Wang J, Fissan H, Pui DYH (2013) Exposure assessment of nanosized engineered agglomerates and aggregates using Nuclepore filters. J Nanopart Res 15:1955
47. Dixkens J, Fissan H (1999) Development of an electrostatic precipitator for off-line particle analysis. Aerosol Sci Technol 30:438–453
48. John AC, Kuhlbusch TAJ, Fissan H (2001) Size-fractionated sampling and chemical analysis by total-reflection X-ray fluorescence spectrometry of PMx in ambient air and emissions. Spectrochim Acta Part B 56:2137–2146
49. Asbach C, Kaminski H, von Barany D, Kuhlbusch TAJ, Monz C, Dziurowitz N, Pelzer J, Vossen K, Berlin K, Dietrich S, Götz U, Kiesling H-J, Schierl R, Dahmann D (2012) Comparability of portable nanoparticle exposure monitors. Ann Occupat Hyg 56:606–621
50. Möhlmann C, Monz C, Neumann V, Dahmann D, Asbach C, Kaminski H, Todea AM (2015) From comparison tests to recommendations in standardisation for counting nanoparticles by using CPCs. Presentation at the international congress on safety of engineered nanoparticles and nanotechnologies, 12–15 April 2015, Helsinki, Finland
51. Fierz M, Houle C, Steigmeier P, Burtscher H (2011) Design, calibration, and field performance of a miniature diffusion size classifier. Aerosol Sci Technol 45:1–10
52. Marra J, Voetz M, Kiesling H-J (2009) Monitor for detecting and assesing exposure to airborne nanoparticles. J Nanopart Res 12:21–37
53. Marra J (2011) Using the Aerasense NanoTracer for simultaneously obtaining several ultrafine particle exposure metrics. J Phys Conf Ser 304:012010

54. Zhang SH, Akutsu Y, Russell LM, Flagan RC, Seinfeld JH (1995) Radial differential mobility analyzer. Aerosol Sci Technol 23:357–372
55. Tritscher T, Beeston M, Zerrath AF, Elzey S, Krinke TJ, Filimundi E, Bischof OF (2012) NanoScan SMPS: a novel, portable nanoparticle sizing and counting instrument. J Phy Conf Ser 429:012061
56. Fonseca AS, Viana M, Querol X, Todea AM, Monz C, Asbach C (2015) Intercomparison of portable (nanoScan) and stationary mobility particle sizers for nanoscale aerosol measurements. In preparation
57. Stabile L, Cauda E, Marini S, Buonanno G (2014) Metrological assessment of a portable analyzer for monitoring the particle size distribution of ultrafine particles. Ann Occup Hyg 58:860–876
58. Steer B, Gorbunov B, Muir R, Ghimire A, Rowles J (2014) Portable planar DMA: development and tests. Aerosol Sci Technol 48:251–260
59. Miller A, Frey G, King G, Sunderman C (2010) A handheld electrostatic precipitator for sampling airborne particles and nanoparticles. Aerosol Sci Technol 44:417–427
60. Fierz M, Meier D, Steigmeier P, Burtscher H (2014) Aerosol measurement by induced currents. Aerosol Sci Technol 48:350–357
61. Leith D, Miller-Lionberg D, Casuccio G, Lersch T, Lentz H, Marchese A, Volckens J (2014) Development of a transfer function for a personal, thermophoretic nanoparticle sampler. Aerosol Sci Technol 48:81–89
62. Thayer D, Koehler KA, Marchese A, Volckens J (2011) A personal, thermophoretic sampler for airborne nanoparticles. Aerosol Sci Technol 45:744–750
63. Azong-Wara N, Asbach C, Stahlmecke B, Fissan H, Kaminski H, Plitzko S, Kuhlbusch TAJ (2009) Optimisation of a thermophoretic personal sampler for nanoparticle exposure studies. J Nanopart Res 11:1611–1624
64. Azong-Wara N, Asbach C, Stahlmecke B, Fissan H, Kaminski H, Plitzko S, Bathen D, Kuhlbusch TAJ (2013) Design and experimental evaluation of a new nanoparticle thermophoretic personal sampler. J Nanopart Res 15:1530
65. Faure B, Dozol H, Brouard C, Guiot A, Clavaguera S (2015) Evaluation of a personal sampler for the assessment of mass-based exposure to airborne nanoparticles. Environ Sci Technol, Submitted
66. Cena LG, Anthony TR, Peters TM (2011) A personal nanoparticle respiratory deposition (NRD) sampler. Environ Sci Technol 45:6483–6490
67. Thongyen T, Hata M, Toriba A, Ikeda T, Koyama H, Otani Y, Furuuchi M (2015) Development of a PM0.1 personal sampler for evaluation of personal exposure to aerosol nanoparticles. Aerosol Air Qual Res 15:180–187
68. Tsai C-J, Liu C-N, Hung S-M, Chen S-C, Uang S-N, Cheng Y-S, Zhou Y (2012) Novel active personal nanoparticle sampler for the exposure assessment of nanoparticles in workplaces. Environ Sci Technol 46:4546–4552
69. Young L-H, Lin Y-H, Lin T-H, Tsai P-J, Wang Y-F, Hung S-M, Tsai C-J, Chen C-W (2013) Field application of a newly developed personal nanoparticle sampler to selected metalworking operations. Aerosol Air Qual Res 13:849–861

Exposure Assessment: Methods

Dirk Dahmann

Abstract At the current state of development, exposure assessment of nanoparticles and their agglomerates and aggregates (NOAA) cannot be regarded as clear and internationally harmonized. Many aspects like metric to be used, nature of background treatment, use of a "tiered approach," and others still need a lot more research and international standardization. This chapter gives some recommendations on planning, execution, and documentation of exposure assessment and suggests some kind of general categorization of the various types.

Keywords Background treatment, Categorization, Metrics, Quality control, Tiered approach

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1 Introduction

Nanotechnology is regarded as one of the key enabling technologies (KET) [1] of our time directly or indirectly influencing a dramatically rising number of products, enterprises, and workers every year. As a consequence, an estimated two million workers will be exposed over approximately the next 10 years [2]. The core reason for these developments is the change in physical, biological, and chemical properties of a given material when its particles' diameters drop into the nanorange of approximately below 100 nm. There has been concern about a connected increase in toxicity of nanoparticles [3, 4], and this does touch all parts of the relevant products' life cycles from production to application/use and finally their waste state. Because of the precautionary principle [5], a lot of research has been successfully performed with respect to all pathways of possible human exposure toward nanoparticles released from nanomaterials [6]. In principle, nanoparticles can be incorporated by ingestion, dermal resorption, and inhalation [7], and during all the stages of the life cycles of the relevant products, they can potentially be released [8]. Whereas gastro-intestinal resorption of nanoparticles is mainly a topic in consumers' protection [9] and the importance of dermal resorption has been identified as probably of secondary importance at least when healthy human skin is concerned, inhalation of airborne nanoparticles is regarded as the most important pathway into the human body [6, 10].

If workers in production, consumers, and finally environmentally exposed populations are discussed [69], the former are currently regarded as the most likely and highly exposed group [11]. As a consequence, this article will mainly concentrate on exposure toward nanoparticles in a workplace environment.

Whereas exposure toward single chemical compounds or, e.g., respirable dust does not generate problems with regard to the definition of the substance to be monitored, measured, or assessed, this is not the case for nanoparticles. Currently, a large international effort is made concerning a proper, useful, and "correct" definition of what nanoparticles or nanomaterials are [12, 13]. This is most important as it is not sufficient to just define a particle diameter range to be regarded [14]. Additionally, the origin of the airborne particles needs to be discussed. Particles in the respective diameter range may come from a "natural" or sometimes also called "urban" background. These particles are largely generated by combustion processes (transportation, domestic or industrial energy production, etc.) and are virtually omnipresent. They are part of the unintentionally produced aerosol (with, e.g., welding fume also belonging into that category) sometimes denominated as containing "ultrafine" particles contrary to the nanoparticle proper which are intentionally produced [13]. In most cases in industrial environments, exposure assessment of intentionally produced nanoparticles is the relevant problem to be solved. Sometimes they are also called engineered nanoparticles in the references [15]. This article will concentrate on exposure toward intentionally produced nanoparticles ("engineered nanoparticles") contrary to the background of unintentionally produced ones. The latter will be called ultrafine particles for clarification [13].

Additionally, the question, of which particle diameter range is to be assessed, is not answered comprehensively, yet. The diameter range of up to 100 nm is a critical one, obviously. In addition, and as many studies have shown, primary particles will more or less readily form aggregates and agglomerates [16] after release into the workplace air. These agglomerates/aggregates have particle diameters of several hundred to above 1,000 nm and are also easily able to reach the human alveolar region (as respirable dust [17]). In the human respiratory tract, they can be deposited. The model of the deposition of airborne particles in the human respiratory tract by the International Commission on Radiological Protection (ICRP) is widely used for the estimation of doses [18] and describes the deposition of particles in the respective diameter range. Therefore, in future exposure assessment of inhaled nanoparticles should also always include their aggregates and agglomerates as well, especially as their stability in the human respiratory tract (surfactant) is not guaranteed [19]. The most recently used term for the analyte in question therefore is NOAA (“nanoparticles and their agglomerates and aggregates” [14, 20]). This term will be used henceforth in this paper when the object of exposure assessment is meant.

A last aspect should be that exposure assessment needs to be put into context within the process of risk management and risk assessment for nanoparticle workplaces [21, 22]. The risk for workers’ health is the ultimate problem to be solved (i.e., minimized). A currently accepted definition is that risk is a function of hazard and exposure [23]. Hazard in this model is basically the particles’ toxicity. And as a consequence, only significant exposure will cause a moderate to high risk for low toxic particles.

Figure 1 shows a very basic graph with this information. For the following discussion of exposure assessment, one always has to keep in mind that exposure (concentration of airborne particles, dose of incorporated particles) is only one aspect of the risk assessment procedure. Always the hazard aspect (i.e., the toxicity of the particle in question) has to be taken into account in addition, for a complete assessment of risk.

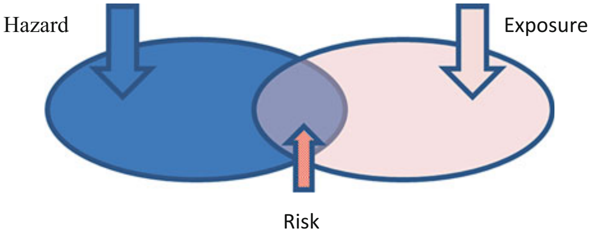

Fig. 1 Risk as a function of hazard (toxicology) and exposure

2 The Aim of Exposure Assessment

In the last years many papers have been published on various aspects of exposure assessment [24–29]. However, depending on the final use of the exposure date collected, several different types of exposure assessments need to be distinguished. This is in the eyes of the author not just an artificial categorization, but it has important consequences for the way the assessments need to be performed.

In this paper three different types of exposure assessments will be distinguished:

Type 1: Assessment in the context of companies' *risk assessment/risk management* procedure
Type 2: Assessment to *test for compliance* of occupational exposure limits (OELs)
Type 3: Assessment in order to *quantify exposure for scientific* (or similar) *purposes*

Table 1 gives some general information on the nature of these different types of exposure assessments. In this table the first column lists a "key question" which is supposedly answered by the respective type of exposure assessment. Column two gives the type of answer obtainable to that question. The next column describes very roughly the type of measurement devices (if any) that can be used, without going into too much detail. Column 4 gives some information on the typical time base of the respective assessments. Columns 5 and 7 do not show differences with respect to the need of well-developed protocols to be followed or the need for background control. These are the same for all three types of exposure assessments. Column 6 gives some information on the estimated degree of instrumentation or measurement personnel required to perform the measurements. A somewhat more detailed discussion is needed, however.

2.1 *Type 1: Exposure Assessment in Order to Check for Suitability of Risk Management/Assessment Procedures in a Company*

According to the modern approach of protecting the safety and health of workers and to legal requirements in many countries, the employer shall use a formalized procedure to identify the risks in his/her company (in our context in connection with the intended use of nanomaterials), to plan and implement measures (technical, organizational, and finally measures of personal protection), and to minimize these risks (e.g., [30]). After implementation, the success of these measures has to be checked. One possible way is in the case of potential inhalation exposure against NOAA, exposure assessment, and comparison of its result with predetermined conditions before the measures have been implemented. This basically means that the potential result is a "yes" or "no" (measures are sufficient or they are not) [31]. Exposure assessment in these cases should make use of readily available sufficiently reliable, quick, and possibly direct-reading instruments

Table 1 Classification of types of exposure assessment depending on the question to be answered

Type of exposure assessments	"Lead question"	Answer	Key requirements for methods	Time base	Protocols	"Ease of use" of instrumentation	Background control
1	"Are measures of risk management sufficient?"	Yes/no	Fast, direct reading, readily available	No pre-requirements, mainly job based/activity based	Follow well-defined procedures	High importance	Highly important
2	"Is an OEL complied with?"	Yes/no	Following approved procedures	Average shift exposure (8 h) PLUS short term (15 min recommended)	Follow well-defined procedures	Fairly high importance	Highly important
3	"How high is exposure/concentration/dose?"	Numerical result	High quality, following well-defined procedures	Average shift exposure (8 h) PLUS short term (15 min recommended)	Follow well-defined procedures	Low importance	Highly important

[32]. Additionally, some sample collection on suitable filter substrates [33] may be required to make sure that the identified elevated (if any) nanoparticle concentrations are really connected to NOAA. Though of course, as in all other cases, quality of data must be sufficient for the task, it is not of the highest concern in these cases. Instead, the data must be quickly available and possibly be generated by the company's own measurement personnel, which requires that the instruments can be operated with moderate requirements for training.

A very important aspect is the time base of measurements. For type 1 assessments, the time base is usually the work process ("task") investigated. No or little concern is necessary for shift exposure, as the employer usually only needs to know whether during the job/activity in question, the exposure concentration is sufficiently lowered by the control measures in place.

In any case, the assessment needs to follow predetermined and well-documented procedures ("protocols"), in order to be of value for the employer [34]. One should always keep in mind that in addition to its relevance for the protection of the workers' health, risk management quite often also means substantial investment for a company. Here, decisions as always need to be based on sound, reliable, and not the least traceable data.

As risk assessment/management only involves those engineered nanoparticles which are handled or synthesized in a company, the need for background discrimination/control in order to prevent ultrafine particles (see above) from falsifying the results is high.

2.2 Type 2: Exposure Assessment with the Intention of Compliance Control

In future it should be expected that legally binding occupational exposure limits will be installed on a respective national base. These have the consequence of defining "safe" exposure conditions (with respect to the health of workers but also in a legal sense for the companies). As they have a very strong impact on companies' activities, exposure assessment in the context of compliance control does have distinctly different properties in some respect.

First of all, in most cases, countries that implement OELs will immediately also have defined the procedure for checking compliance of these OELs. In the European Union, e.g., new OELs immediately define some general requirements for quality of their exposure assessment (measurement) procedures. These are currently defined in EN 482 [35].

EN 482 gives (in its Table 2) general requirements for the so-called expanded uncertainty of a method (a combination of the random and nonrandom errors attributable to these measurements). As an example, the expanded uncertainty for a compliance control measurement procedure should be below 50% in a range of above a tenth and half of the respective threshold limits (i.e., OELs). In some

Table 2 Source domains of NOAA exposure according to 46

Source domain #	Description	Typical workplaces/ exposure scenarios	Some generally assumed properties of NOAA
1	Production/synthesis	Emissions from the reactor, leaks through seals and connections, incidental releases	Discrete nanoparticles and/or homogeneous and inhomogeneous agglomerates
2	Handling/transfer	Collection, harvesting, bagging	Mostly agglomerates
		Bag dumping, bag emptying, scooping, etc.	
		Weighing	
		Dispersion compounding in composites	
3	Use/application	Pouring, injection molding, (jet) milling, stirring, mixing	Usually of mixed composition
		Application of coatings or spraying of solutions	
4	Fracturing and abrasion of manufactured nanoparticle-enabled end products	Low-energy abrasion, manual sanding	Multi-composed aerosols
	End of life applications	High-energy machining, e.g., sanding, grinding, drilling, cutting, shredding	Also matrix-bound nanoparticles

respect compliance control also only requires the answering of a yes or no question. However, because of the legal consequences of these assessments/measurements in many cases, a lot more requirements need to be fulfilled to demonstrate that an OEL is complied with by exposure measurements [36]. As usually compliance control assessment is done with spot measurements, which describe conditions of exposure found at the date of these measurements, but is supposed to answer the question whether there is a guarantee that the OEL is complied with under *all possible conditions* in the respective workplace; normally, one measurement is simply not enough to reliably answer the question. In fact, sampling/measurement strategy gains a very high importance in these types of exposure assessments, and a statistical approach (i.e., several repetitions of measurements in the same workplace) is usually needed to produce a high enough level of reliability [37].

An important difference to the type 1 assessments is the time base of compliance measurements. When in type 1 the job/activity ("task") defines the duration of measurements, in the legal environment their external comparability becomes all important. Therefore, in most cases, only shift (i.e., 8 h) average exposure concentrations will be comparable to the OELs. Additionally, in many cases, short-term ("peak") exposure concentrations become important. Whereas 8 h is the worldwide accepted duration of a shift, for short-term exposures, a generally accepted definition is missing. However, 15 min seem to be a good compromise and are recommended here. These 15-min-short-term measurements should contain the suspected period of highest exposure. The task's duration itself is not of prime importance for the planning of these measurements.

Needless to say, background control is mandatory for compliance measurements as well. A general discussion of how to do this will be given a little later in this paper.

2.3 Type 3 Assessment: Quantification of Exposure for Scientific (and Similar) Purposes

It could be argued that every type of exposure assessment is intended to generate quantitative data, i.e., information on the exact height of concentration of engineered nanoparticles in the air in a given workplace. However, this exact number is relevant over the whole range of concentration and also, e.g., below a given threshold limit or OEL only in cases where it is used as a base for further decisions. This is of course the case in epidemiological research, when dose–response functions are to be determined also in so-called low-dose ranges, to eventually find threshold limits of effect. It could, e.g., also be relevant in cases of potential industrial diseases, when individual dose of a worker has to be determined for compensation questions.

In almost all cases, dose cannot be determined directly but has to be calculated from averaged concentration data and time weighing. A direct consequence of this is that all type 3 assessments should also have the shift as a time base. Though it is possible to recalculate average shift exposures from increments of several exposure episodes based on jobs/activities, a direct determination of the complete shift should be preferred. In the end a good estimate of historical dose of engineered nanoparticles is only possible when the average shift exposure is known. This is true for epidemiological and for compensation determination purposes [38].

Additionally, when quantitative assessment/measurement of the concentration of engineered nanoparticles is performed, the necessity to follow well-defined protocols is very high. In fact, it is quite likely that future reevaluation of data will be required, as new knowledge about the mechanisms of action of the harmful agents in question (here the engineered nanoparticles) is generated [39]. The more is known about the exact protocols, which have been used for exposure assessment, the more valuable "historical" exposure data will be for their future reevaluators.

As it can be expected that these data are generated by well-trained and selected technicians, in most cases, the need to apply "easy-to-use" instruments is less explicit as in the first two cases of exposure assessment described before.

Reality shows, however, that as the probability to collect funding for really well-designed type 3 measurement campaigns decreases rapidly in an environment of competing (and mostly also expensive) "other" projects, epidemiologists will be forced to use data from type 1 or type 2 measurements as a surrogate for high-quality type 3 data. Of course this will give rise to a variety of possible errors.

If, for example, compliance measurements are used for these purposes (as they are at least in most cases already shift averages), the underlying measurement strategy should be discussed very carefully [40]. To check compliance in workplaces, in some countries, a so-called worst case strategy is used. This means that in a given company, the workplaces with potentially the highest exposure are preselected and assessed for compliance control purposes. If data from these workplaces are used to estimate average exposure, an overestimation of exposure could result with dose–response thresholds being estimated as too low. The contrary is true, when data from exposure assessment would be used from a "climate of measuring at the low end" (in order to demonstrate general compliance, which would in practice not be existing). In these cases epidemiologists would underestimate exposure and end up, e.g., with a too high dose–response threshold.

Again, well-defined protocols of the measurements will be able to clarify the situation and help epidemiological science to properly discuss and control exposure uncertainties.

3 Methods of Exposure Assessment

In general terms there are two possibilities to assess (determine) exposure concentrations in workplaces: they can be directly measured or they can be estimated by calculation, also called modeling.

As there are different chapters of this handbook dealing in depth with the various methods employed in this context, some general remarks must here be sufficient. It is generally quite feasible to calculate exposure concentrations for classic components like gases, organic molecules, or heavy metals when their source concentration and the conditions of ventilation are well known [57]. A lot of research has been published in this respect during recent years. For engineered nanoparticles, two difficulties arise here. First, their source (emission) concentration is generally not known beforehand, and second, the aerosols change rapidly once released into the workplace air, by physical processes like agglomeration and aggregation, by adsorption of gaseous components present there, or by chemical reactions (as their very nature makes them more reactive than larger particles). Nevertheless, modeling of exposure concentration is a promising and well-developed part of exposure assessment [41–45].

A novel approach for the modeling of exposures to NOAA was developed a few years ago [46]. It suggested to group the possible exposure scenarios into basically four different so-called source domains. Table 2 gives a short description of these domains and their consequences. The authors suggested to use the model as a starting point for refinement.

Several tools for estimating the exposure to NOAA have been developed like CB Nanotool [47], NanoSafer [48], ANSES [49], and Stoffenmanager Nano [50]. All of them are meant to allow for qualitative or semiquantitative assessment of NOAA exposure developed from basic information and as a rough first estimate. They are classic tools for control banding.

Still, exposure assessment by various measurement techniques is currently the heart of the matter and will be discussed elsewhere in this handbook.

However, when the decision to perform exposure assessment as one of the described three types above has been taken, a lot more needs to be decided upon, before actual work can start. This makes exposure assessment for engineered nanoparticles markedly different from classical work in the field of say chemical compounds or respirable and inhalable dust.

While for the latter compounds, the question of the metric to be used is basically solved beforehand, e.g., by looking at the respective OEL in the country in question [51], this is definitely not the case for engineered nanoparticles. Almost in all cases of chemical substances, their mass concentration (or in the case of gases in the volume concentration) is the target metric. Marked exceptions exist, e.g., for asbestos and related fibers, where the number of "critical" fibers has to be "counted" in a predefined volume of air. What is a "critical" fiber (i.e., the so-called WHO fibers) has been defined in a fairly long process of international consensus building [52] and depends basically on (sometimes changing) toxicological evidence. How these fibers are counted, i.e., what measurement and sampling instrumentation has to be used, is also fairly well agreed upon in the international scientific community [53].

For engineered nanoparticles the question of which metric to be used (i.e., mass, surface, number concentrations) is still not resolved, at least not from toxicological science [14]. Until some internationally well agreed upon recommendations, hopefully founded by toxicological evidence [19], appear, there is some uncertainty here, which force the assessor to make well-founded decisions. If that is done, the choice should be discussed, and some reasons, why the particular metric(s) has (have) been chosen, should be given. Other chapters of this handbook will give some suggestions as to what metric may be the most appropriate. Depending on the type of exposure assessment described above, more or less effort needs to be put into the selection process. If, for example, just the suitability of risk management procedures needs to be checked, simply the availability of instrumentation may be a good reason for a choice of the metric. In the case of type three measurements, especially for determination of dose–response functions, the choice of the metric will be a crucial one [54].

As always, the choice of the measurement strategy to be employed is very important [14, 55]. However, in this field, a lot of experience from classical chemical component assessment may be used. In fact, there are already international standards available which describe aspects of measurement strategy readily usable for engineered nanoparticles as well [36]. In order to optimize the return on investment for the exposure assessment and to allow for a suitable use of available instrumentation and personnel, a so-called tiered approach, especially for type 1 and type 2 measurements, is recommended (see below). More on this special aspect is given in this chapter. Once again, it is very important to recollect that depending on the type of measurement (see above), different measurement strategies will have to be used. If, for example, the efficiency of a certain local exhaust ventilation has to be checked within the scope of risk management in a company, a much less sophisticated measurement strategy will be necessary compared to the one used for assessment of exposure of the workers active in that particular workplace, if their quantitative shift exposure for epidemiological purposes or for OEL compliance control is needed.

A very important point for each type of exposure measurements is the role of the contextual information. As always, all those aspects of the actual workplace, which could possibly influence the actual height of exposure concentrations (e.g., intensity of work, availability and actual use of technical protective measures, temperature, ventilation, etc.), need to be documented to complete the results of exposure assessment. For engineered nanoparticles, a very important special point is the discussion and documentation of all aspects of background concentration. These will be discussed in a later part of this chapter. It can be a very good idea to develop a scheme for the documentation of these factors. Some research projects have published proposals for these, but in almost all cases, these need to be adapted for the special purposes of the own measurement campaign and its demands [34].

The same is basically true for reporting of the results of the exposure assessment. It cannot enough be stressed that a full documentation of not only the results but also the contextual information and especially all decisions taken in the design and performance of the assessment needs to be done. This, being always true in general, is especially relevant for the field of engineered nanoparticles as we currently cannot draw upon a wealth of generally agreed upon procedures and, in simply every measurement campaign, a lot of individual decisions have to be taken.

4 The Background Problem

As mentioned before, exposure assessment of engineered nanoparticles faces a specific problem as there is virtually always a quite substantial background concentration of ultrafine particles, mainly resulting from various combustion purposes, present [16, 24]. They typically have particle mobility diameters of below 100 nm. Their concentration range in an urban setting can be assumed to reach several thousand particles per cubic centimeter but can easily be even higher. These particles are present in outdoor air, but they are also generated from indoor (in-company) sources [56]. Thus, it is very important to control conditions with respect to this aspect. In addition to engine exhaust (forklifts, lorries, etc.), tobacco smoke aerosol or the emissions of certain electrical engines can be relevant as well.

Beside the physical problems of dealing with these measurement problems, which will be discussed a little later, there is also the problem of a definition of the term background. Thus, for example, in type 2 exposure assessment for compliance control purposes, the distinction of background concentrations (for which the employer is *NOT* responsible) from "real" exposure concentrations (which he/she has to control and treat in risk management) may even become a legal problem. An example of the definition of "background exposure" is given in the German TRGS 402[1] [57]. This definition is regarded as helpful but may not be acceptable in other countries. So a check of the respective definition may be necessary before exposure assessment starts.

The possible ways to deal with the background problem can be grouped as follows:

Primarily, all the "known external sources" of ultrafine particles generated within the respective company (intentionally or unintentionally) should be closed as reasonably possible. This means that all tobacco smoking should be prevented, and air ventilation from tobacco smoking areas should be excluded during measurements. All traffic from combustion engines (e.g., forklifts) should be directed away from the measurement areas if possible.

In addition to the active control of external sources, all possible emission events during the course of the measurements should be registered and documented together with the time when they happened in a "diary of events" ("log"). Together with a monitoring instrument giving a continuous plot of exposure results, significant cross sensitivities can so be identified and possibly corrected for. Also, this helps to identify eventual significant increases in exposure concentration ("peaks"), which are indicated by monitoring instruments and for which external sources of ultrafine particles have not been recorded.

Last, the correction for the omnipresent background of ultrafine particles has to be done. Several attempts to do just this have been published as of lately [7, 24, 58]. They all try to measure the background concentrations in addition to the real workplace exposure during activities (see definition above). This can be done on parallel (i.e., during the exposure measurement proper) or by separation of the time periods for background measurements and exposure measurements, however, both at the site of actual production. In the latter case, background measurements could be performed during work/production, but excluding the very process which is intended to be assessed. Note that in this case, different procedures which would also give rise to emissions of engineered nanoparticles in the same company would be regarded as "background." The same is also true when a parallel measurement approach is chosen. In these cases, there is a "near-field" (or personal) exposure measurement and a "far-field" one. For the latter it is assumed that concentrations will basically be attributable to the background. In all cases the separate determination of the ultrafine aerosols outside the production building is recommended, as this concentration, which is basically the "urban background," can vary considerably during activities and the variations cannot be explained by the abovementioned external identifiable sources. Comparison of outside air concentration to inside background once again is also a simplification, and some authors have tried to

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[1] "The background exposure should be understood as the air concentration which would be present at the location of the activities involving hazardous substances if these activities were not being carried out."

solve this problem by determining the "transfer function" of outside air concentrations to inside (workplace) air during production-free times. They would use the transfer function for recalculation of exposure concentrations recording the outside concentration in addition to and on parallel to the exposure assessment proper. This process can become very demanding concerning time and resources and is another reason to try to simplify the process of exposure determination for engineered nanoparticles without sacrificing quality [7].

The simplest way to control the background of ultrafine particles in the presence of airborne NOAA is of course the direct and selective measurement of these NOAA. Unfortunately, there are currently almost no practical methods available in this respect. While the recently published method for determination of the mass of carbon nanotubes (CNT) by using a special temperature program of the original NIOSH method for determining elemental carbon from diesel exhaust [59] can be regarded as an example of selective determination of the NOAA CNTs, that method suffers from a fairly low sensitivity, as the published limit of detection would translate into a very large number-based ("fibers/cm^3") exposure. There have recently also been some suggestions on possible selective NOAA determinations like catalytically active metals or by making use of spectroscopic methods on sampled NOAA, but up to now no "market ready" solutions have materialized [60]. As a consequence, background control currently remains one of the most problematic aspects of NOAA exposure assessment.

5 Minimizing Cost and Effort Without Loss of Quality: The Tiered Approach

Keeping in mind the old paradigm of analytical chemistry to measure the necessary and not the possible and, additionally, the many side parameters of NOAA exposure assessment, already mentioned, there is a very important need to minimize cost and effort especially for type 1 assessments within the scope of risk/assessment/risk management – without losing "too much" quality. Several years before, so-called tiered approaches were proposed, to solve the problem of getting enough reliable and fast information on the risk management process without the need of taking high-cost measurement equipment and many measurement technicians into EACH respective workplace for several days to get the necessary information [31, 34, 62, 70].

Basically, all these stepped (or "tiered") procedures suggest that at first, the respective workplaces are evaluated making use of available documents, like material safety data sheets, production process descriptions, physical properties of the materials in use or produced, etc. When this "initial assessment," as it is occasionally called, would result in the possibility of NOAA exposure, a second step or "basic assessment" would have to be performed. This basic assessment would make use of direct-reading equipment ("monitoring"), using personal devices with either number concentration or surface area concentration as a metric, adequately (but not extensively) trained personnel and possibly some accompanying sampling of particles on a suitable substrate for subsequent qualitative analysis ("sampling"). The latter would intend to identify, whether NOAA actually have been present during work activities. Depending on the nature of the NOAA in question, a variety of methods could be used for that purpose, like electron microscopy in connection with qualitative spectroscopic analysis or wet-chemical analysis (i.e., ICP/MS techniques after digestion of the samples). As described above, monitoring would be performed with and without control measures in place to identify easily and directly, whether those have been sufficient.

The outcome of this "basic" or tier 2 assessments could be one of the three following:

1. Exposure assessment was *inconclusive*:

   Insufficient information on the nature/quantity of the risk is available/was obtained. More and better techniques for assessment are needed.

2. Exposure assessment was *conclusive – risk management measurements are not sufficient*:

   In that case additional measures have to be implemented, and exposure assessment has to be repeated subsequently (possibly again using tier 2 procedures initially).

3. Exposure assessment was *conclusive – risk management measurements are sufficient*:

   In that case, document the outcome of the exposure assessment, and enter the normal repetition cycle of risk assessment procedures in the particular company.

In the first outcome, a final so-called expert assessment would be needed [34]. This tier 3 assessment would make use of much more elaborate equipment like particle size distribution measurements, sampling for different mass-based analytical techniques, etc. More on the nature of these measurements can be found in different chapters of this handbook.

A generalized schematic of this procedure can be seen in Fig. 2. Note that more substructured approaches than using just three tiers have been proposed. For example, the initial assessment already could contain more than one step (tier), with a subdivision into purely document-oriented work, and some very preliminary workplace observations using, for example, handheld instruments. This does not change the principle, however.

From Fig. 2 it can also be seen that at several points in the flowchart, decisions have to be taken. This easily constitutes the most critical point of the procedure, as solid decision criteria are needed to guarantee "correct" selection of options. There are already several proposals available in the references for some of these [34, 61, 62]. This paper is not able to discuss all aspects of the proposed sets of criteria in depth. However, the consequences of "wrong" decisions need a short treatment.

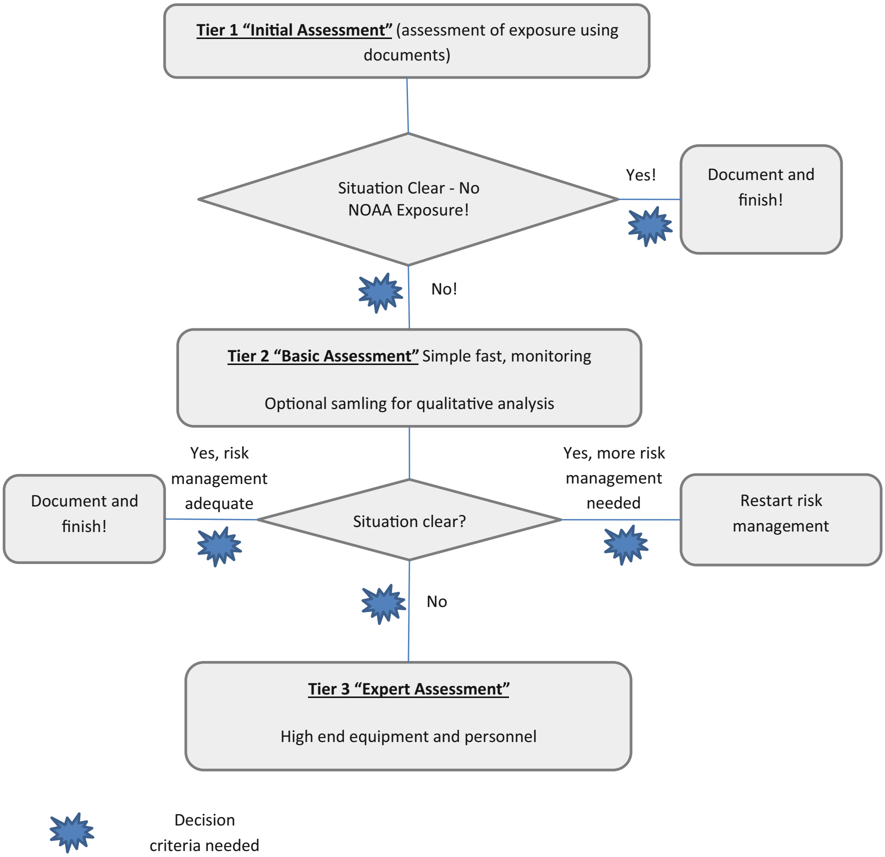

Fig. 2 Schematic of a simple tiered approach

The most important decision would probably have to be taken after a tier 2 basic assessment campaign. Was sufficient information gathered to make a decision concerning the success of risk management? Let us assume that this answer was positive. The outcome "Yes, we know enough. Risk management was not appropriate!" will probably result from some "significant" increase in NOAA concentration (with the metric number or surface area) compared to the background. Here, a false-positive result would cause a wrong decision. It would "only" cause additional expenses by the company in making further investment necessary. In the second unambiguous outcome ("Yes, information was sufficient. Risk management was adequate"), a false-negative result would be possible. In that case, some risk to workers' health will not have been recognized.

As in both cases wrong decisions do have important consequences (especially, in the second case), there is some tendency recognizable toward the third exit out of this problem. The decision that not enough information was obtained to make a decision is quite tempting. This would, however, counteract the intention of a tiered approach. A solution out of this dilemma could be to increase the quality of the information obtained from the "basic assessment." This can be done by simply repeating the process, say two times, or by following a strict and predetermined protocol, i.e., a standard operation procedure (SOP) [34]. The role of these SOPs will be discussed a little later in more depth. It needs to be stressed once again that the *hazard* of the NOAA in question has to play a significant role in the process of deciding whether *enough* information is available. For example, in the case of exposure to rigid high-aspect-ratio carbon nanotubes (CNTs), the decision to accept a basic assessment as "proof" that no significant exposure was detected will be much harder to take than in the case of a nano-clay agglomerate NOAA. This paper can give no universally valid criteria for the decisions mentioned above. References hold some recommendations, however. Only future regular practice will show whether and which set(s) of decision criteria will work.

At the time of writing this paper, the European Commission has mandated standardization work in the field of evaluating the tiered approach [63]. Hopefully, in a few years more experience will be ready for publication.

6 Minimizing Cost and Effort Without Loss of Quality: NEAT

Already in 2006, NIOSH has proposed a very similar approach to reduce cost and effort for NOAA determination by introducing the NEAT (nanoparticle emission assessment technique) concept [64, 65]. It was developed as an initial step to semiquantitatively evaluate emissions in nanomaterial workplaces and consists of a combination of field portable, direct-reading instrumentation (DRI), and filter-based air sampling with subsequent laboratory analysis. It did include not only a set of "simple" and fast tools like direct-reading equipment but was also an offer to companies to use the resources of a task force at NIOSH specifically installed for this purpose. In addition to provide exposure information, the system was also intended to provide information on the nature and effectiveness of the NEAT approach itself. At the very time of publication of this handbook, a major revision of the NEAT procedure is prepared at NIOSH ("NEAT 2.0") which is intended to take the experience gained from the first NEAT into account, modify the procedure, and provide more robust information. As NEAT 2.0 is currently simply not available in written form, no detailed discussion is possible at the time being. Readers are encouraged, however, to closely watch the novel approach and the accompanying publications.

7 General Recommendations and the Role of Standardization

As may have been evident from the previous pages, exposure assessment of NOAA is by no means a currently clear and predetermined procedure. Many different cases and subcases exist. Measurement procedures are available, none of them clearly "recommended" (or even mandatory).

Each and every exposure assessment campaign demands a great number of highly significant decisions to be taken by the planners, the measurement technicians, and the evaluators. Some very general hints have been given in this text, but as currently no off-the-shelf standard operation procedures are available for all these cases, some recommendations are nevertheless possible.

1. *Clarify* for yourself and together with the other experts involved in the particular assessment campaign, what *the purpose* of this campaign is (epi-study, risk assessment/risk management, compliance control).
2. Whatever you do, *follow* some written and *documented protocol* (standard operation procedure, SOP). If you do not find one in the references, write one for your specific purpose and follow it as closely as possible during your assessment campaign
3. If you use measurement techniques, make sure that all necessary quality control steps have been taken and documented [66–68] (a critical review of these aspects will be given elsewhere in this handbook).
4. Gather as much *information* (before and during assessment) on the nature of the nanostructured material and the NOAA(s) as well as the w*orkplaces* you want to assess, and document them.
5. Try to investigate the *nature* (i.e., quality and quantity) *of the background* during your assessment as closely as possible. This would probably include data logging over the complete measurement period using direct-reading instruments plus writing a "diary" of significant events and attributing these to specific events in your log.
6. If you follow a tiered approach (see above), use your *predetermined decision criteria* on the quantitative data you have gathered and give a qualified recommendation.
7. *Document* each of your *decisions* to allow for a subsequent reevaluation of your data together with these data. This does include documentation of "primary" measurement data.

As mentioned before, the European Union has mandated several European standards to facilitate the situation and give hard and sustainable information on what to do and how. In the context of this chapter, one project is of special importance.

A European standard with the working title "Workplace exposure – Assessment of inhalation exposure to nano objects, and their agglomerates and aggregates" [63] is currently being developed. There will be a detailed discussion on many of the problems mentioned in this text and probably some hard recommendations as well within that document. The project does involve pre-normative research which will in this case consist of extensive modeling of existing sets of measurement data, for example, with the purpose of testing various decision criteria between different steps of a tiered approach (see above). The publication of this standard is expected for 2016.

8 Conclusions

As has been shown, the very nature of exposure assessment for NOAA can be very different, depending on the purpose, exposure data are used for. As a consequence, one is well advised to use a considerable amount of time and resources for the proper planning of the respective campaign.

Once purpose has been clarified, the next step should be selection or writing of a suitable standard operation procedure (or “protocol”) for the intended activities, which needs to be followed closely during the campaign.

A mandatory part of exposure data quantification, be it by measurement or by modeling (which of course could also make use of certain measurement data), must be an intelligent treatment of the respective background.

During and after measurements/modeling, all relevant decisions taken need to be thoroughly documented, in order to allow for a later reevaluation of the data.

If exposure assessment is performed for the purpose of risk assessment/risk management, the use of a “tiered approach” (see above) is advisable. In this case the respective decision criteria for moving on within the tiered approach decision tree or out of it need special care. In any case, decisions *are* encouraged, but the hazard (toxicity) of the NOAA in question must be taken into considerations at this stage.

Last but not least, a very important aspect needs mentioning.

The intention behind exposure assessment always should be to be *relevant*. Though this does sound a little bit strange, as no measurement technician or modeling expert would ever start with the purpose of gathering irrelevant data, unfortunately, many of the data obtained do end with the label “irrelevant.” This is especially true in the field of NOAA exposure assessment. For example, if an extensive measurement campaign of NOAA concentrations (possibly using various different measurement devices with particle number concentration plus surface concentration as target metric) does not provide information on the respective background, then these extensive (and expensive!) data may end up as irrelevant, because the information in question is simply not provided.

On the other hand, a fairly simple exposure assessment using simple well-selected direct-reading instruments providing a data log on the exposure period together with a detailed diary of what happened within that time period MAY be quite relevant, in order to allow answering the question: “Is workers’ health in danger in the workplaces in question or not?”

References

1. European Commission (2011) High-level expert group on key enabling technologies – final report. http://ec.europa.eu/enterprise/sectors/ict/files/kets/hlg_report_final_en.pdf. Accessed 03 Mar 2015
2. Roco MC (2003) Broader societal issues of nanotechnology. J Nanoparticle Res 5:181–189
3. Oberdörster G, Oberdörster E, Oberdörster J (2005) Nanotoxicology: an emerging discipline evolving from studies of ultrafine particles. Environ Health Perspect 113:823–839
4. Nel A, Xia T, Mädler L et al (2006) Toxic potential of materials at the nanolevel. Science 311:622–627
5. Scientific Committee on Emerging and Newly-Identified Health Risks SCENIHR (2007) Opinion on the appropriateness of the risk assessment methodology in accordance with the technical guidance documents for new and existing substances for assessing the risks of nanomaterials. http://ec.europa.eu/health/ph_risk/committees/04_scenihr/docs/scenihr_o_004c.pdf. Accessed 04 Mar 2015
6. Savolainen K, Alenius H, Norppaa H et al (2010) Risk assessment of engineered nanomaterials and nanotechnologies—a review. Toxicology 269:92–104
7. Kuhlbusch TAJ, Fissan H, Asbach C (2009) Nanotechnologies and environmental risks – measurement technologies and strategies. In: Linkov I, Steevens J (eds) Nanomaterials: risks and benefits. Springer, Berlin, pp 233–243
8. Sajid M, Ilyas M, Basheer C et al (2015) Impact of nanoparticles on human and environment: review of toxicity factors, exposures, control strategies, and future prospects. Environ Sci Pollut Res 22:4122–4143
9. Kessler R (2011) Engineered nanoparticles in consumer products: understanding a new ingredient. Environ Health Perspect 119:A120–A125
10. Staroňová K, Nielsen JB, Roursgaard M, Knudsen LE (2012) Transport of SiO2 nanoparticles through human skin. Basic Clin Pharmacol Toxicol 111:142–144
11. Methner M, Hodson L, Geraci C (2008) Nanoparticle emission assessment technique (NEAT) for the identification and measurement of potential inhalation exposure to engineered nanomaterials — part A. J Occup Environ Hyg 7:127–132
12. European Commission M/461 (2009) Mandate addressed to CEN, CENELEC and ETSI for standardization activities regarding nanotechnologies and nanomaterials. http://ec.europa.eu/growth/tools-databases/mandates/index.cfm?fuseaction=search.detail&id=443#. Accessed 4 Aug 2015
13. ISO TR 27628 (2007) Workplace atmospheres – ultrafine, nanoparticle and nano-structured aerosols – inhalation exposure characterization and assessment. International Organization for Standardization, Geneva
14. Brouwer DH, Lidén G, Asbach C, Berges M, Van Tongeren M (2014) Monitoring and sampling strategy for (manufactured) nano objects agglomerates and aggregates (NOAA). In: Vogel U et al (eds) Handbook of nanosafety – measurement, exposure and toxicology. Elsevier, London, Waltham, San Diego
15. Savolainen K (2014) General introduction. In: Vogel U et al (eds) Handbook of nanosafety – measurement, exposure and toxicology. Elsevier, London, Waltham, San Diego
16. Kuhlbusch TAJ, Neumann D, Fissan H (2004) Number size distribution, mass concentration and particle composition of PM1, PM2.5, and PM10 in bag filling areas of carbon black production. J Occup Environ Hyg 1:660–671
17. EN 481 (1993) Workplaces atmospheres: size fraction definitions for measurement of airborne particles. European Committee for Standardization
18. ICRP (1994) Human respiratory tract model for radiological protection, 1st edn. Ann ICRP 24 (1–3), International Commission on Radiological Protection, p 1–482
19. Alenius H, Catalán J, Lindberg H et al (2014) Nanomaterials and human health. In: Vogel U et al (eds) Handbook of nanosafety – measurement, exposure and toxicology. Elsevier, London, Waltham, San Diego

20. ISO/TS 12901-1 (2012) Nanotechnologies – occupational risk management applied to engineered nanomaterials – part 1: principles and approaches. International Organization for Standardization, Geneva
21. Berges M, Aitken R, Sheona AK, Savolainen K, Luotamo M, Brock T (2014) Risk assessment and risk management. In: Vogel U et al (eds) Handbook of nanosafety – measurement, exposure and toxicology. Elsevier, London, Waltham, San Diego
22. NanoCare (2009) Health related aspects of nanomaterials final scientific report. http://www.nanopartikel.info/files/projekte/NanoCare/NanoCare_Final_Report.pdf. Last accessed 17 July 2015
23. National Research Council (NRC) (1983) Risk assessment in the federal Government: managing the process. Committee on the Institutional Means for Assessment of Risks to Public Health. http://www.nap.edu/catalog/366/risk-assessment-in-the-federal-government-managing-the-process. Last accessed 13 July 2015
24. Kuhlbusch TA, Asbach C, Fissan H, Göhler D, Stintz M (2011) Nanoparticle exposure at nanotechnology workplaces: a review. Part Fibre Toxicol 8:22
25. Nanzarenko Y, Lioy PJ, Mainelis G (2014) Quantitative assessment of inhalation exposure and deposited dose of aerosol from nanotechnology-based consumer sprays. Environ Sci Nano 1:161–171
26. Kim B, Kim H, Yu IJ (2014) Assessment of nanoparticle exposure in nanosilica handling process. Ind Health 52:152–162
27. Shepard MN, Brenner S (2014) An occupational exposure assessment for engineered nanoparticles in semiconductor fabrication. Ann Occup Hyg 58:251–265
28. Chen SC, Wang J, Fissan H, Pui DYH (2013) Exposure assessment of nanosized agglomerates and aggregates using Nuclepore filter. J Nanoparticle Res 15:10
29. Dahm MM et al (2013) Occupational exposure assessment in carbon nanotube and carbon nanofiber primary and secondary manufacturers: mobile direct-reading sampling. Ann Occup Hyg 57:328–344
30. Verordnung zum Schutz vor Gefahrstoffen (Gefahrstoffverordnung) (Decree on the protection against hazardous substances). Federal Ministry of Labour and Social Affairs, Federal Republic of Germany. Last changed 3 Feb 2015. http://www.baua.de/de/Themen-von-A-Z/Gefahrstoffe/Rechtstexte/pdf/Gefahrstoffverordnung.pdf;jsessionid=FCC59845EACCCB2625CAD35E397E7BB6.1_cid333?__blob=publicationFile&v=14. Accessed 4 Aug 2015
31. VCI – German Chemical Industry Association (2011) Exposure measurement and assessment of nanoscale aerosols. https://www.vci.de/vci/downloads-vci/tiered-approach.pdf. Last accessed 13 July 2015
32. nanoIndEx (2015) Assessment of individual exposure to manufactured nanomaterials by means of personal monitors and samplers (report in preparation). http://www.nanoindex.eu/. Accessed 8 Aug 2015
33. Bard D, Thorpe A, Wake D et al (2008) Investigations of methods for the sampling of airborne nanoparticles by electron microscopy. Inhaled Particles X, Sheffield
34. NanoGEM (2012) Standard Operation Procedures for assessing exposure to nanomaterials, following a tiered approach. http://www.nanogem.de/cms/nanogem/upload/Veroeffentlichungen/nanoGEM_SOPs_Tiered_Approach.pdf. Last accessed 13 July 2015
35. EN 482 (2012) Workplace exposure – general requirements for the performance of procedures for the measurement of chemical agents. European Committee for Standardization
36. EN 689 (1995) Workplace atmospheres – guidance for the assessment of exposure by inhalation to chemical agents for comparison with limit values and measurement strategy. European Committee for Standardization
37. Clerc F, Vincent R (2014) Assessment of occupational exposure to chemicals by air sampling for comparison with limit values: the influence of sampling strategy. Ann Occup Hyg 58:437–449

38. Dahmann D, Taeger D, Kappler M et al (2007) Assessment of exposure in epidemiological studies: the example of silica dust. J Expo Sci Environ Epidemiol 18:452–461
39. Dosemeci M, McLaughlin JK, Chen J-Q et al (1995) Historical total and respirable silica dust exposure levels in mines and pottery factories in China. Scand J Work Environ Health 21 (Suppl 2):39–43
40. Attfield MD, Hearl FJ (1996) Application of data on compliance to epidemiological assessment of exposure–response: the case of data on exposure of United States coal miners. Occup Hyg 3:177–184
41. Seipenbusch M, Binder A, Kasper G (2008) Temporal evolution of nanoparticle aerosols in workplace exposure. Ann Occup Hyg 52:707–716
42. Koivisto AJ, Yu M, Hämeri K, Seipenbusch M (2012) Size resolved particle emission rates from evolving indoor aerosol system. J Aerosol Sci 47:58–69
43. Peters TM, Heitbrink WA, Evans DE et al (2006) The mapping of fine and ultrafine particle concentrations in an engine machining and assembly facility. Ann Occup Hyg 50:249–257
44. Asbach C, Dahmann D, Kaminski H et al (2009) In: Kuhlbusch TAJ, Krug H, Nau K (eds) NanoCare – health related aspects of nanomaterials. Dechema, Frankfurt, pp 74–88
45. Brouwer DH, Duuren-Stuurman B, Berges M et al (2009) From workplace air measurement results towards estimates of exposure? Development of a strategy to assess exposure to manufactured nano-objects. J Nanoparticle Res 11:1867–1881
46. Schneider T, Brouwer DH, Koponen IK et al (2011) Conceptual model for assessment of inhalation exposure to manufactured nanoparticles. J Expo Sci Environ Epidemiol 21:450–463
47. CB nanotool 2.0 (2015) http://controlbanding.net/Services.html. Last accessed 14 July 2015
48. NanoSafer 1.01 (2015) http://nanosafer.i-bar.dk/. Last accessed 14 July 2015
49. ANSES (2014) https://www.anses.fr/en. Last accessed 14 July 2015
50. Soffenmanager Nano (2015) https://nano.stoffenmanager.nl/. Last accessed 14 July 2015
51. International Labour Organisation (ILO) Chemical exposure limits. http://www.ilo.org/safework/info/publications/WCMS_151534/lang--en/index.htm. Last accessed 16 July 2015
52. WHO (1985) Reference methods for measuring airborne man-made mineral fibres. Copenhagen. Environmental health report no. 4, World Health Organization Regional Office for Europe
53. WHO (1997) Determination of airborne fibre number concentrations a recommended method, by phase-contrast optical microscopy (membrane filter method). World Health Organization, Geneva
54. Maynard AD, Aitken RJ (2007) Assessing exposure to airborne nanomaterials: current abilities and future requirements. Nanotoxicology 1:26–41
55. Brouwer D, Berges M, Virji MA et al (2012) Harmonization of measurement strategies for exposure to manufactured nano-objects; report of a workshop. Ann Occup Hyg 56:1–9
56. Dahmann D, RiedigerG SJ et al (2001) Intercomparison of mobility particle sizers (MPS). Gefahrstoffe–Reinhalt Luft 61:423–427
57. (German) Committee on Hazardous Substances, TRGS 402 (2010) Identification and assessment of the risks from activities involving hazardous substances: inhalation exposure, last modified 4/2014 available in English language. http://www.baua.de/en/Topics-from-A-to-Z/Hazardous-Substances/TRGS/pdf/TRGS-402.pdf?__blob=publicationFile&v=3. Last accessed 16 July 2015
58. Tsai C-J, Huang C-Y, Chen S-C et al (2011) Exposure assessment of nano-sized and respirable particles at different workplaces. J Nanoparticle Res 13:4161–4172
59. NIOSH (2013) Current Intelligence Bulletin 65 department of health and human services Centers for Disease Control and Prevention National Institute for Occupational Safety and Health Occupational exposure to carbon nanotubes and nanofibers. http://www.cdc.gov/niosh/docs/2013-145/pdfs/2013-145.pdf. Last accessed 17 July 2015
60. NANODEVICE (2013) Novel concepts, methods, and technologies for the . . . the measurement and analysis of airborne engineered nanoparticles in workplace air. Final report. http://cordis.europa.eu/publication/rcn/16648_en.html. Last accessed 17 May 2015

61. Witschger O, Le Bihan O, Reynier M et al (2012) Recommendations for characterizing potential emissions and exposure to aerosols related from nanomaterials in workplace operations. Hygiene et Securite du Travail 226:41–55
62. McGarry P, Morawska L, Morris H et al (2012) Measurements of particle emissions from nanotechnology processes, with assessment of measuring techniques and workplace controls, Safe Work Australia. http://www.safeworkaustralia.gov.au/sites/SWA/about/Publications/Documents/714/Measurements_Particle_Emissions_Nanotechnology_Processes.pdf. Last accessed 17 May 2015
63. European Commission Mandate M/461, item #13 CEN WI00137053 – workplace exposure – guidance document of assessment of exposure to inhaled manufactured nanoparticles (working title, in preparation). European Committee for Standardization
64. Methner L, Hodson M, Geraci C (2009) Nanoparticle emission assessment technique (NEAT) for the identification and measurement of potential inhalation exposure to engineered nanomaterials — part A. J Occup Environ Hyg 7:127–132
65. Methner L, Hodson M, Dames A, Geraci C (2009) Nanoparticle emission assessment technique (NEAT) for the identification and measurement of potential inhalation exposure to engineered nanomaterials – part B: results from 12 field studies. J Occup Environ Hyg 7:163–176
66. Horn H-G, Dahmann D, Asbach C (2014) Quality control of measurement devices – what can be done to guarantee high-quality measurements? In: Vogel U et al (eds) Handbook of nanosafety – measurement, exposure and toxicology. Elsevier, London, Waltham, San Diego
67. Kaminski H, Kuhlbusch TAJ, Rath S et al (2013) Comparability of mobility particle sizers and diffusion chargers. J Aerosol Sci 57:156–178
68. Todea AM, Beckmann S, Kaminski H, Asbach C (2015) Accuracy of electrical aerosol sensors measuring lung deposited surface area. J Aerosol Sci (in print)
69. OECD Environment Directorate (2015) Analysis of the survey on available methods and models for assessing exposure to manufactured nanomaterials. Series on the Safety of Manufactured Nanomaterials No. 56. Organization for Economic Co-operation and Development. http://www.oecd.org/officialdocuments/publicdisplaydocumentpdf/?cote=env/jm/mono%282015%2920&doclanguage=en. Accessed 4 Aug 2015
70. OECD Environment Directorate (2015) Harmonized tiered approach to measure and assess the potential exposure to airborne emissions of engineered nano-objects and their agglomerates and aggregates at workplaces. Harmonized Series on the Safety of Manufactured Nanomaterials No. 55. Organization for Economic Co-operation and Development. http://www.oecd.org/officialdocuments/publicdisplaydocumentpdf/?cote=env/jm/mono%282015%2919&doclanguage=en. Accessed 4 Aug 2015

Occupational Release of Engineered Nanoparticles: A Review

Ehsan Majd Faghihi and Lidia Morawska

Abstract Characterising the release of different types of engineered nanoparticles (ENPs) from various processes is of critical importance for the assessment of human exposure, as well as understanding the possible health effects of these particles. Therefore, the main aim of this chapter is to present a comprehensive review of studies which report on the release of airborne ENPs in different nanotechnology workplaces. The chapter will cover topics of relevance to the occupational characterisation of ENP emissions, ranging from the identification of different particle release sources and scenarios to measurement methods and working towards a more uniform approach to characterisation. Furthermore, a brief review of ENP exposure control strategies, together with the application of mathematical modelling as an effective tool for the characterisation of emissions at nanotechnology workplaces, is included.

Keywords Airborne particle release, Engineered nanoparticles, Nanotechnology, Workplace measurement

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1 Introduction: Release of Engineered Nanoparticles in the Workplace

Engineered nanoparticles (ENPs) are usually defined as particles with a non-agglomerated size smaller than 100 nm, emitted from various activities. Characterising the release of ENPs during all stages of their life cycle is crucial to our understanding of their behaviour and fate in different environments. This knowledge can then be applied to assess human exposure to ENPs, as well as to develop adequate management and regulation strategies. Figure 1 shows the life cycle of nanomaterials, from synthesis through to their use and recycling. Depending on factors such as manufacturing, environmental conditions, and use of the product, the release of nanomaterials (including ENPs) can occur at any or all of these stages [1]. Due to their small size, these particles will often remain in the air for a long time, creating significant opportunities for occupational as well as environmental exposure.

1.1 Release Scenarios for Engineered Nanomaterials (ENMs)

In a review paper by Gottschalk and Nowack [3], four scenarios were put forwards to categorise the release of engineered nanomaterials (ENM) into the environment

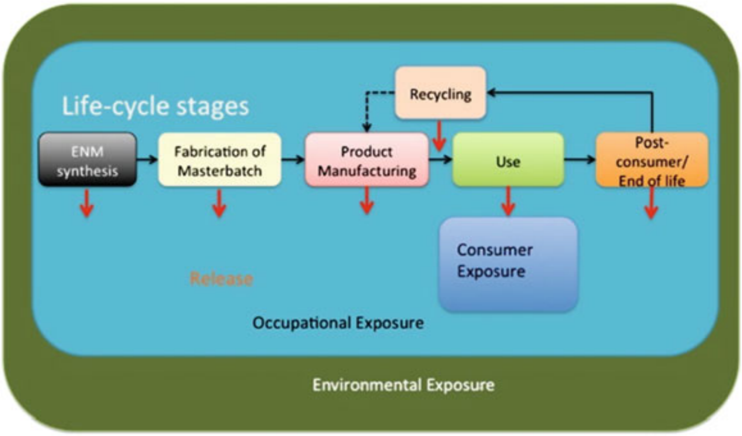

Fig. 1 Life cycle of products containing ENPs [2]

(including soil, water and air). These scenarios are release during production, release from manufacturing processes, release from products (e.g. intended release from ENM-containing sunscreen or unintended release by degradation or abrasion of the product), and finally release from technical compartments (e.g. wastewater treatment plants). For all of these scenarios, it is essential to understand the factors responsible for the release of ENMs, as well as the concentration and fate of the released nanomaterials.

According to the literature, ENPs are most likely to be released during synthesis and handling (the first two stages). This highlights the importance of occupational measurements of airborne particles, where various activities/processes in relation to ENPs take place. However, release can also occur during the "use" phase, where it is influenced by environmental factors such as humidity, pressure, UV radiation and human activities, and also during the "post-use" phases, where release is mainly driven by the waste treatment of products containing these materials, as well as environmental factors [2].

1.2 Activities Contributing to the Release of Engineered Nanoparticles in the Workplace

Table 1 shows examples of the most common sources of occupational ENP emissions.

According to Hämeri et al. [4], the majority of ENP emissions are due to particle formation through nucleation and condensation. Hot processes such as metal refining and processing, as well as different types of combustion, can generate particles of a small-size and large-size surface area. The primary size of these particles (often 10–50 nm) is largely a function of the generating conditions (i.e. production in open [5] or closed [6, 7] process). Following their release, the particles coagulate at different rates, based on their concentration, as well as other less significant factors, such as type of material and activity. For example, particles emitted from welding coagulate much more rapidly compared to those generated by metal refining, which tend to remain in the nanosize range. Coagulation leads to the formation of large agglomerates – sometimes beyond the nanosize range – which exhibit similar biological behaviour to nanoparticles upon deposition in the respiratory tract [4]. There is a large body of literature available investigating ENP release and exposure during the production of a broad range of material types, including carbon nanotubes (CNTs) and fullerenes [8–11], metals and their oxides [12, 13, 8, 14, 15, 9] and nanocomposites [16].

The synthesised material may also be released and become airborne during the handling and refinement phase, which includes activities such as opening and cleaning the reactor [17], filtering [7], drying [13], palletising [6], grinding and milling [17, 18]. Nanomaterials in a dry powder form may also be released as agglomerates and possibly discrete particles during uncontrolled handling and

Table 1 Examples of the most common sources of ENP emission at workplaces [4]

Aerosol process and type	Emission source
Hot processes	Metal refining
	Galvanising
	Welding
	Metal cutting
	Thermal spray coating
	Cooking
Combustion	Diesel engines
	Gasoline engines
	Gas-based engines
	Incineration (e.g. power plants, heating)
	Gas-fired heating
Indoor air quality-related aerosols	Office machinery
	Cleaning fluids
	Building materials
	Infiltration of ambient nanoaerosols
Mechanical processes	High-speed metal grinding and machining
	High-energy drilling
Flame-based powder generation	Carbon black production
	Ultrafine TiO_2 production
	Fumed silica production
	Fumed alumina production
Nanotechnology	Carbon nanotube production
	Gas-phase generation of ENPs
	Nanoparticle powders
	Sprays from engineered nanoparticle suspensions and solutions

transfer. The rate of particle release from dry powder depends on the degree of agitation during handling, as well as the physical and chemical nature of the powder [4]. Studies conducted by Evans et al. [19], Kuhlbusch et al. [6] and Maynard et al. [20] investigated this phenomenon; however, release from the bagging and shipping of ENM-containing suspensions has not been yet studied.

A very broad range of activities are involved in the processing of free nanomaterials or those embedded in a solid matrix, including mixing powders in liquids, drying, drilling, cutting, sanding, thermal and high-energy processes, rolling, folding, etc., basically, any activity capable of modifying the polymer structure of the material [2]. The probability of releasing embedded nanoparticles during handling is relatively low; however, being subject to high mechanical and thermal energy may lead to particle release. In 2013, the Commonwealth Scientific and Industrial Research Organisation (CSIRO) published a report [21] on the emission of ENMs from a range of different materials, including composites from several machining processes. It was concluded that a combination of primary nanoparticles, including matrix particles with embedded nano-objects, free reinforcing nano-objects (e.g. nanoparticles, nanofibres and nanoclays) and particles from the matrix itself, is emitted during such activities.

The focus of previous studies investigating the release of ENPs in the workplaces was not merely limited to activities contributing to particle release. Other important parameters, such as ENP type (e.g. metals and their oxides [22, 13, 15], carbonaceous materials [23, 19, 9], composites [24–27]) and form (i.e. single, aggregated/agglomerated and embedded in a matrix), have been the subject of many recent studies.

2 Characterisation of the Release of Engineered Nanoparticles in Nanotechnology Workplaces

2.1 Instruments and Techniques

The wide range of physiochemical properties of ENPs, as well as the lack of a single instrument/method capable of measuring them, calls for a multi-metric approach using a range of measurement instruments, when characterising workplace release/exposure. Depending on their working principles, measurement instruments can be classified in different ways. For instance, O'Shuaghnessy [28] divided them into "time-integrated" and "direct-reading" categories. In time-integrated devices, particles are collected on filters and then subjected to further analysis, in order to determine their concentration. According to the National Institute for Occupational Safety and Health (NIOSH), these devices can be used to sample "total" dust and "respirable" dust. On the other hand, direct-reading instrument is used to measure the real-time concentration (mass or number) and size distribution of ENPs. In an extended classification scheme, Kuhlbusch et al. [29] also considered time and particle size and divided the available devices into four classes:

- Class I: size-resolved, time-resolved instruments whose particle detection capability is based on optical or electrical mobility, such as the Scanning Mobility Particle Sizer (SMPS) [30, 31], Fast Mobility Particle Sizer (FMPS) [32–34], Optical Particle Counter (OPC) [35–37] and Electrical Low-Pressure Impactor (ELPI) [38, 39].
- Class II: size-integrated, time-resolved instruments, such as the Condensation Particle Counter (CPC) [30, 36] and Nanoparticle Surface Area Monitor (NSAM) [40, 41]. The former gives a signal weight to each of the detected particles, whereas the signal strength in the latter is proportional to the squared diameter of the detected particle.
- Class III: size-resolved, time-integrated instruments, such as the Low-Pressure Cascade Impactor and the Micro-Orifice Uniform Deposit Impactor (MOUDI) [42, 43]. The major drawbacks associated with this class are possible significant changes in the size distribution of particles due to the high-pressure difference

inside the instrument and changes in physiochemical characteristics of the particles due to interactions with one another or the gas.
- Class IV: size-integrated, time-integrated methods that mainly rely on sampling particles from a few nanometres to several micrometres in size, such as the electrostatic precipitator and thermal precipitator. Sampling efficiency is greatly influenced by particle size and could deteriorate in very small sizes (<20 nm) due to the diffusion in sampling line or inlet system. Following particle collection on appropriate substrates, common methods to determine bulk chemical composition, morphology (electron microscopy [44, 43]) and single chemical composition analysis (energy-dispersive X-ray [40, 31]) are usually applied.

2.2 Measurement Strategies

As a general rule, cost-effectiveness and relatively high sensitivity of the measurement devices should be considered in any study aiming to characterise ENP release in the workplace. A widely accepted strategy for workplace measurements, which satisfies both conditions fairly well, is the “tiered approach”. NIOSH developed a tiered approach called “NEAT” (Nanoparticle Emission Assessment Technique) [45] that recommends using a handheld device to measure particle number concentration in the first instance, in order to locate the possible release points of ENPs. The main reason for choosing particle number concentration for the initial monitoring is the relatively high sensitivity of this metric in detecting nanoparticles. To confirm the release of ENPs in a location, the tiered approach states that an increase in number concentration compared to the background level should be significant and greater than the error margin of the handheld measurement device. Once the release is confirmed, the tiered approach suggests carrying out more detailed measurements. The tiered approaches proposed and/or developed for the workplace characterisation of ENPs are not limited to NEAT and include several other techniques, such as those developed by the British Standard Institution (BSI) [46] and the German Chemical Association (VCI) [47]. They also consist of a preliminary assessment of the process/activity using handheld measurement devices, followed by an extended assessment if any significant release is detected. The focus of this extended assessment may vary depending on the objectives of the study. For example, in terms of personal exposure studies, it is necessary to combine the real-time data from personal or area devices with the information obtained from people’s activity patterns in the workplace, in order to determine their personal exposure to ENPs. In process-related studies, a measurement suite including more sensitive devices than those used for the preliminary assessment would be placed close to the activity, while in toxicological/epidemiological studies, it would be necessary to use a broad range of measurement and sampling devices in order to obtain the health-relevant metrics, since the best metric/s for measuring the health effects of ENPs are yet to be determined.

One of the biggest challenges in characterising ENP release in the workplace is to differentiate them from the ambient and ultrafine particles originating from natural or incidental sources inside or outside the workplace. To overcome this problem, various approaches have been used in occupational exposure studies, including time series analysis and spatial analysis. Time series analysis is based on an assumption that the concentration measured during the “no work” period is associated with background particles, while any increase in concentration during the “work” period is caused by the process, the particles of interest or both. In the spatial analysis approach, a background measurement site is chosen reasonably far from the process/activity location, where the measured concentration represents the background particles. Therefore, any difference between the process and background concentrations is associated with the process and the particles of interest. Kuhlbusch et al. [29] reported that a majority of the published studies paired a combination of the above approaches, with the addition of chemical/morphological analysis to definitively discriminate ENPs from background particles, since all available online measurement devices are only capable of carrying out this task according to a particles size.

2.3 Findings from the Workplace Measurements

There are a significant number of published studies on ENP release and exposure in various nanotechnology workplaces. Table 2 summarises the findings of the most recent studies. A review of the published work shows that most of these studies used particle number concentration, mass concentration and sometimes particle number size distribution to distinguish ENPs from background aerosols. Among these metrics, number concentration, either measured directly by a CPC or indirectly from size distribution data, was used in almost all workplace measurements as a good indicator of particle release. This is mainly due to the relatively low cost and easy operation of the measurement devices, as well as their high sensitivity in detecting nanoparticles. The downside of using this metric in workplace measurements is the poor comparability of the results, due to different size ranges across different models and the lack of a defined lower size detection limit, especially when a significant contribution from very small particles (<10 nm) is suspected.

Another common metric, size distribution, was reported to be difficult to interpret in several workplace studies, due to bimodal and even multimodal distributions observed in many of the studies. For instance, Koponen et al. [48] measured the size distribution of the emitted particles from a sanding process and reported five modes, with different sizes, ranging from 10 nm to 2 μm. Those in the nanosize were assumed to be due sources other than the particles of interest, such as the machinery motor, vacuum cleaning, oil mist, etc. [49]. In most of the reviewed studies, the presence of large agglomerates or aggregates of the released particles was observed and reported, rather than single primary particles. Another problem associated with measuring particle size distribution in workplace characterisation studies is the

Table 2 Findings of the recent occupational ENP exposure studies (adapted from Kuhlbusch et al. [29])

Workplace	Activity	Material	Measured quantities	Conclusion(s)	Reference
Industrial production	Bagging	Carbon black	PNSD (15–675 nm) PMC PNC CC	No significant release of ENPs Release of agglomerates (>400 nm)	[6]
Industrial production	Production Palletising	Carbon black	PNSD (15–675 nm) PMC PNC CC	Significant release of ENPs and agglomerates in case of leak Significant effect of other sources on PNC	[7]
Toner and printing ink industry	Emptying powder bags	Fumed silica	PNSD (<1 μm) PNC ASA Morph CC	Significant increase in PNC (>100 nm) and ASA confirmed by TEM	[50]
Industrial manufacturing plant	Packaging Palletising	Carbon black	PNSD (<1 μm) SA (<1 μm)	Higher measured values during activity period	[51]
Industrial manufacturing	Liquid process Drying Grinding Handling	Silver	PNSD (15–675 nm) Morphology	Significant release of ENPs and agglomerates in all steps upon opening the machines	[13]
Industrial production	Wet milling	Metal oxides	PNC (0.01–1 μm) MC Morphology	Airborne particles are dominated by other sources Handling of nanomaterials releases particles Larger than several hundred nm	[52]

Industrial production	Bagging Vacuum cleaning	Fullerenes	PNSD (0.15–10 µm) Morphology	Release of ENPs during both activities	[10]
Industrial production	Production Processing	Carbon nanofibres	PMC PNC ASA CO/CO_2	Significant release of ENPs and agglomerates	[19]
Primary and secondary industrial manufacturing	Harvesting Weighing Handling Sonicating Extruding	MWCNT	PNC PMC (respirable) SA Morph EC	No clear link between direct-reading instruments (DRI) results to EC or microscopy data DRIs; weak in quantifying exposure, helpful for control evaluation	[53]
Industrial facility	Chemical Mechanical Planarisation	Metal oxides	PNSD (0.01–5 µm) PNC PMC Morphology	Insignificant increase of ENPs above background level	[54]
Small-scale manufacturer	Production Processing	MWCNT	EC Morphology PMC (respirable) PNC	The highest emission of CNT-containing particles during production	[55]
Manufacturing facility	Synthesis Harvesting Vacuum cleaning	SWCNT	PNSD (0.01–32 µm) PNC SA CO/CO_2 Morphology	Release of SWCNT mainly during harvesting SWCNT releases from background sources such as oil mist and atmospheric photochemical smog particles Release of SWCNT aggregates 1–10 lm from the arc plasma synthesis	[35]

(continued)

Table 2 (continued)

Workplace	Activity	Material	Measured quantities	Conclusion(s)	Reference
Industrial facility	Abrasion	Epoxy/CNT nanocomposite	PNSD Morphology PNC	Increase in released particles' size by increasing the nano-filler content Confirmed emission of free-standing individual CNTs and agglomerates was confirmed	[56]
Pilot factory	Separation Packaging	Al_2O_3	PNSD (0.15–10 μm) Morphology PNC PMC (respirable) SA	Significant release of agglomerates (~305 nm) at separation locations Signs of primary nanoparticles (21–26 nm) release during periods of unstable production Significant release of agglomerates (~90 nm) during packaging	[57]
	Dry and wet abrasive machining	CNT-containing composites	PNSD (0.005–20 μm) Morphology PNC PMC (respirable)	High release during dry cutting Neither individual nor bundled CNT observed in the collected electron microscopy samples	[58]
Upscaling factory	Synthesis Cleaning	SWCNT	PNSD (0.01–10 μm) PNC CO/CO_2 Morphology	Unable to quantify SWCNT emissions due to low concentration CO concentrations; a good indicator of SWCNT emissions Analysis of TEM grids; the only direct method to detect SWCNTs in workplace air	[59]

CC chemical composition, *ASA* active surface area, *SA* surface area application of electrically or optically equivalent diameters in measurement devices, which might not be relevant for nonspherical particles [29].

A review of the published studies also illustrates the advantages and disadvantages of other measurement devices and methods in characterising the release of ENPs in nanotechnology workplaces. For instance, mass concentration measurements, including personal filtration samplers, were found to be insensitive to particles in the nanosize range. Similarly, while surface area has been found to be directly linked to toxicological mechanisms and its measurement techniques are practical in the workplace, they are progressively less sensitive towards smaller particle sizes.

A majority of the studies included background measurements, albeit using different approaches, as discussed in Sect. 2.2. For example, Fujitani et al. [10] and Bello et al. [58] used time series analysis, whereas Demou et al. [5] and Tsai et al. [22] used a spatial analysis approach. In most cases, the obtained results, either in terms of number concentration or size distribution, were used as a base for comparison. Again, the review shows that there was no common approach across the published studies to distinguish activity-related particles from the background. Calculating ratios of particle size distribution, subtracting average pre- and post-activity concentrations, and analysis of variance are among the approaches applied in different studies [50]. Most of the studies used offline electron microscopy, paired with single-particle chemical analysis, to discriminate particles of interest from the background particles. Despite not being overly quantitative, this is currently the only reliable method for the unambiguous identification of ENPs at workplace.

2.4 Towards a More Uniform Characterisation Approach

As illustrated in the previous section, most of the studies conducted on particle release and exposure in nanotechnology workplaces did not attempt or were unable to appropriately address key issues, such as measurement uncertainty and the detection limits of the devices and methods used. Furthermore, a lack of comparability between the results obtained in different release/exposure studies, which is mainly due to (1) the broad range of devices/metrics used in workplace measurements (as shown in Table 2) and (2) the absence of a common procedure for data evaluation, calls for a more uniform approach to the facilitate the characterisation of ENP release and exposure in nanotechnology workplaces. This approach should be able to (1) link the elevated concentrations at the measurement locations to the particles of interest and (2) provide quantitative results. To address this need, Brouwer et al. [60] developed a strategy which includes guidelines on minimum data requirements, the differentiation of ENPs from background particles and, finally, data evaluation and presentation:

1. The minimum set of data required: in any release/exposure characterisation study, it is crucial to take into account the environmental (workplace) conditions while also measuring the physical, chemical and physiochemical properties of the particles. Therefore, the results obtained from both online reading instruments and offline analysis should be paired with workplace information. For real-time measurements, it is recommended to include particle number concentration data, due to its high sensitivity in the nanosize range, as well as either the number size distribution or surface area, when feasible. Where the direct measurement of size distribution and surface area is not practical, particle number concentration for at least two size bins (<100 and >100 nm) should be measured [60]. The morphology and elemental composition of ENPs should also be qualitatively assessed and the results should be included in the dataset. It is also suggested that the "wet" mass concentration of the respirable mass fraction (if applicable) be added to the dataset.
2. Differentiating ENPs from background particles: as previously stated, in order to adequately characterise ENP release/exposure in the workplace, it is crucial to differentiate these particles from background particles that originate from natural or incidental sources inside or outside the workplace. Therefore, in any measurement campaign, the characterisation of background particles should be taken into consideration in the study design stage. This strategy recommends that, before choosing any differentiation technique, several parameters should be considered, including the objectives and timeframe of the measurements, the availability of the instruments and the environmental conditions (e.g. ventilation, presence of other incidental sources of particles). The approach applied for the discrimination of ENPs from background particles, as well as the presence of any potential source of other particles, should be clearly described and documented. It is also recommended to contrast statistically representative size distributions of background particles and those generated by the process/es under investigation.
3. Analysing and reporting the data: according to this strategy, the most important post-measurement steps in the assessment of ENP release/exposure include (but are not limited to) the appropriate processing and analysis of real-time measurement data, benchmarking the performance of the measurement instruments and consistently reporting the results from offline methods. The real-time data should be checked for log-normal distribution, as well as partial autocorrelation and stationarity. Then, summary statistics for the data, such as geometric mean (GM); geometric standard deviation (GSD), as an indication of log-normal distribution; and arithmetic mean (AM), or peak exposure for disease mechanisms – should be extracted [61]. Other useful summary statistics that should be obtained and reported include task-related exposure and the 95% confidence interval. Any real-time measurement devices need to be compared, in terms of size range, averaging time and principle of operation, in order to quantify any difference in their response which may affect the measurements and data analysis. Instead of using conventional, inefficient methods to assess the instrument agreement, such as the Pearson correlation coefficient or paired *t*-test, other

approaches should be used, such as the concordance correlation coefficient (CCC) [62], which is based on the method of variance components. In addition to real-time data, this strategy proposes a protocol for reporting the results of offline analysis as well. For electron microscopy results in particular, it is recommended to report the type of the instrument, the properties of the filter and/or grid (including its coating and pore size), how uniformly the deposited particles are distributed on the substrate, the number of deposited particles on the substrate for each collected sample and the magnification level of the microscope, as well as the different types of observed particle morphology and shape (such as free, agglomerate, spherical, etc.). It is also recommended by Pfefferkorn et al. [63] to include, if possible, a comparison of the real-time size distribution with one reconstructed from TEM images, in order to confirm the online measurement data. Finally, this strategy discusses the need for developing a database, which allows data pooling for the purpose of further analysis, calibration or validation of exposure models and also for building exposure scenarios [60].

Despite recent attempts to develop a more uniform assessment approach for characterising ENP occupational emission and exposure, there is still a need for further improvement. Firstly, a consensus must be reached over the metric that best represents the possible health effects of ENPs. Furthermore, quantifying the sensitivity of ENP emissions to all of the influencing parameters, such as material, type of activity and conditions in the workplace, should be considered, as it will improve the physical characterisation of particle emissions.

3 Exposure Control in Nanotechnology Workplaces

It is unanimously agreed that controlling the emission of such particles from different indoor sources is the most effective way to reduce exposure and avoid their potentially harmful health effects. The major issue with regard to the safety of personnel who are exposed to ENPs is to minimise their exposure time as much as possible. Taking this principle into account at the development and design stage for any nanotechnology process, followed by incorporation of the necessary health and safety considerations into other phases, such as implementation and operation, can guarantee minimisation of exposure to ENPs [64]. In general, ENP exposure control approaches are divided into three main categories: engineering control, administrative control and personal protective equipment (PPE) [65]. These approaches can be considered based on the risk of exposure at any particular workplace, which in turn depends on several parameters, including duration of the measured activity, as well as quantity and type of the nanomaterial of interest.

The engineering control approach relies on implementing necessary changes in the workplace and to the process of interest, as well as eliminating and substituting hazardous nanomaterials at the identified source(s) of particle emission, with the aim of reducing exposure to ENPs. To do this, the emission source can be enclosed and/or the personnel can be isolated in controlled spaces. Another effective engineering control strategy is adequate ventilation in the workplace. In addition to maintaining a suitable temperature, if used efficiently, ventilation can play a key role in controlling the exposure of workers to ENPs. There are a broad range of techniques that can be used for this purpose, from point-source ventilation to full-room ventilation [66]. Hämeri et al. [4] showed that nanosized particles were effectively cleaned and exhausted from the breathing zone as a result of using the "displacement flow" principle. Based on this principle, cool and fresh air is supplied at low velocity to the floor level of the workplace, reaching the breathing zone without any major mixing with the warm and contaminated air, and pushes the small particles up to the ceiling, where they are exhausted.

To minimise worker exposure to ENPs, administrative control measures also need to be implemented to complement and reinforce the engineered controls. The most important administrative control task is training personnel and updating them with current information regarding potential hazards, safe work procedures, personal hygiene, regular housekeeping, etc. [64]. Additionally, it should be ensured that the transfer, labelling and storage of nanomaterials (either hazardous or nonhazardous) are done in accordance with the applicable standard procedures. As another important administrative measure, the number and duration of shifts worked by personnel in contact with nanomaterials should be minimised.

PPEs including respirators, gloves, glasses and various clothing are considered as the last line of defence against exposure to ENPs, when the application of engineering and administrative controls is not feasible or they fail to provide the necessary protection. For activities that require working with dry nanomaterials or handling any type of nanomaterials in the absence of other effective control measures, a respirator is recommended. According to NIOSH, the same protective clothing required for wet chemistry laboratory (i.e. lab coat, long pants, long-sleeved shirts and enclosed footwear) is recommended for the handling of nanomaterials. Eye protection is also recommended, depending on the type and level of the hazard; however, it should also be noted that conventional protective eyewear is not effective against dry airborne ENPs.

Among the abovementioned measures, engineering controls are favoured as they are implemented closest to the source/s and are least dependant on worker behaviour and involvement.

4 Modelling: An Approach to Quantify ENP Emissions

A major objective in the indoor characterisation of particles is to differentiate particles of different origins from one another [4]. A significant challenge to overcome is that ambient particles are mixed with particles from the process/es of interest, which makes it very difficult to differentiate them. To solve this problem, a mathematical modelling approach can be used to find the key descriptive parameters that influence the emission and behaviour of emitted particles in the workplace.

Such models rely on mass-balance equations to describe the dynamic behaviour of indoor particles and take into account processes such as penetration, filtration and infiltration that govern the concentration of ambient particles introduced into the indoor environment [67]. Another important factor is the source of aerosol particles entering the workplace and the types of indoor activities carried out. Introducing the effects of these factors into the mass-balance equation facilitates quantification of the emission rates of particles during the activity/activities of interest. There are different approaches to quantify emission rates, including analytical and semiempirical methods. For semiempirical approaches, the Multi-Component Size-Resolved Indoor Aerosol Model (MC-SIAM) developed by Hussein et al. [68] was applied to a number of indoor aerosol measurement scenarios and proven to be effective. The main advantage of this approach is the ability to calculate the emission rate as a function of particle size and time. However, in order to ensure a reasonable accuracy of this approach, there are certain requirements to meet with regard to the quality of aerosol measurements, as well as the characteristics of indoor air flow [4].

Modelling can be a very useful tool for differentiating measured particles according to their source, as well as understanding their dynamic behaviour, transport and fate in nanotechnology workplaces. The knowledge obtained from such models could greatly contribute to obtaining a more accurate estimation of the exposure to ENPs, as well as minimising the associated health risks.

References

1. Upadhyayula VKK, Meyer DE, Curran MA, Gonzalez MA (2012) Life cycle assessment as a tool to enhance the environmental performance of carbon nanotube products: a review. J Clean Prod 26:37–47. doi:10.1016/j.jclepro.2011.12.018
2. Nowack B, David RM, Fissan H, Morris H, Shatkin JA, Stintz M, Zepp R, Brouwer D (2013) Potential release scenarios for carbon nanotubes used in composites. Environ Int 59:1–11. doi:10.1016/j.envint.2013.04.003
3. Gottschalk F, Nowack B (2011) The release of engineered nanomaterials to the environment. J Environ Monitor 13(5):1145–1155. doi:10.1039/c0em00547a
4. Hämeri K, Lähde T, Hussein T, Koivisto J, Savolainen K (2009) Facing the key workplace challenge: assessing and preventing exposure to nanoparticles at source. Inhal Toxicol 21 (s1):17–24. doi:10.1080/08958370902942525
5. Demou E, Peter P, Hellweg S (2008) Exposure to manufactured nanostructured particles in an industrial pilot plant. Ann Occup Hyg 52(8):695–706. doi:10.1093/annhyg/men058
6. Kuhlbusch T, Neumann S, Fissan H (2004) Number size distribution, mass concentration, and particle composition of PM1, PM2. 5, and PM10 in bag filling areas of carbon black production. J Occup Environ Hyg 1(10):660–671
7. Kuhlbusch TAJ, Fissan H (2006) Particle characteristics in the reactor and pelletizing areas of carbon black production. J Occup Environ Hyg 3(10):558–567. doi:10.1080/15459620600912280

8. Methner M, Hodson L, Dames A, Geraci C (2010) Nanoparticle emission assessment technique (NEAT) for the Identification and measurement of potential inhalation exposure to engineered nanomaterials – part B: results of 12 field studies. J Occup Environ Hyg 7:163–176
9. Yeganeh B, Kull CM, Hull MS, Marr LC (2008) Characterization of airborne particles during production of carbonaceous nanomaterials. Environ Sci Technol 42(12):4600–4606. doi:10.1021/es703043c
10. Fujitani Y, Kobayashi T, Arashidani K, Kunugita N, Suemura K (2008) Measurement of the physical properties of aerosols in a fullerene factory for inhalation exposure assessment. J Occup Environ Hyg 5(6):380–389
11. Tsai S-J, Hofmann M, Hallock M, Ada E, Kong J, Ellenbecker M (2009) Characterization and evaluation of nanoparticle release during the synthesis of single-walled and multiwalled carbon nanotubes by chemical vapor deposition. Environ Sci Technol 43(15):6017–6023. doi:10.1021/es900486y
12. Demou E, Stark WJ, Hellweg S (2009) Particle emission and exposure during nanoparticle synthesis in research laboratories. Ann Occup Hyg 53(8):829–838. doi:10.1093/annhyg/mep061
13. Park J, Kwak BK, Bae E, Lee J, Kim Y, Choi K, Yi J (2009) Characterization of exposure to silver nanoparticles in a manufacturing facility. J Nanoparticle Res 11(7):1705–1712
14. Wang J, Asbach C, Fissan H, Hülser T, Kuhlbusch TJ, Thompson D, Pui DH (2011) How can nanobiotechnology oversight advance science and industry: examples from environmental, health, and safety studies of nanoparticles (nano-EHS). J Nanoparticle Res 13(4):1373–1387. doi:10.1007/s11051-011-0236-z
15. Möhlmann C, Welter J, Klenke M, Sander J (2009) Workplace exposure at nanomaterial production processes. In: Journal of Physics: conference series, 2009. IOP Publishing, p 012004
16. Tsai S-J, Ashter A, Ada E, Mead JL, Barry CF, Ellenbecker MJ (2008) Control of airborne nanoparticles release during compounding of polymer nanocomposites. Nano 3:301–309. doi:10.1142/S179329200800112X
17. Kuhlbusch T, Kaminski H, Jarzyna D, Fissan H, Asbach C (2011) Measurements of nanoscale TiO_2 and Al_2O_3 in workplace environments-methodology and results. JOEH
18. Faghihi EM, Martin D, Clifford S, Edwards G, He C, Asbach C, Morawska L (2014) Are there generalizable trends in the release of airborne clay nanoparticles from a jet milling process? Aerosol Air Qual Res, (Article in Press). doi:10.4209/aaqr.2014.06.0124
19. Evans D, Ki Ku B, Birch M, Dunn K (2010) Aerosol monitoring during carbon nanofiber production: mobile direct-reading sampling. Ann Occup Hyg 54(5):514–531
20. Maynard AD, Baron PA, Foley M, Shvedova AA, Kisin ER, Castranova V (2004) Exposure to carbon nanotube material: aerosol release during the handling of unrefined single-walled carbon nanotube material. J Toxicol Environ Health A 67(1):87–107
21. CSIRO (2013) Investigating the emissions of nanomaterials from composites and other solid articles during machining processes. CSIRO, Safe Work Australia, Canberra
22. Tsai S-JC, Ada E, Isaacs JA, Ellenbecker MJ (2009) Airborne nanoparticle exposures associated with the manual handling of nanoalumina and nanosilver in fume hoods. J Nanoparticle Res 11(1):147–161
23. Johnson DR, Methner MM, Kennedy AJ, Steevens JA (2010) Potential for occupational exposure to engineered carbon-based nanomaterials in environmental laboratory studies. Environ Health Perspect 118(1):49
24. Cena LG, Peters TM (2011) Characterization and control of airborne particles emitted during production of epoxy/carbon nanotube nanocomposites. J Occup Environ Hyg 8(2):86–92
25. Methner M, Crawford C, Geraci C (2012) Evaluation of the potential airborne release of carbon nanofibers during the preparation, grinding, and cutting of epoxy-based nanocomposite material. J Occup Environ Hyg 9(5):308–318. doi:10.1080/15459624.2012.670790

26. Raynor PC, Cebula JI, Spangenberger JS, Olson BA, Dasch JM, D'Arcy JB (2011) Assessing potential nanoparticle release during nanocomposite shredding using direct-reading instruments. J Occup Environ Hyg 9(1):1–13. doi:10.1080/15459624.2012.633061
27. Mazzuckelli LF, Methner MM, Birch ME, Evans DE, Ku B-K, Crouch K, Hoover MD (2007) Identification and characterization of potential sources of worker exposure to carbon nanofibers during polymer composite laboratory operations. J Occup Environ Hyg 4(12): D125–D130
28. O'Shaughnessy PT (2013) Occupational health risk to nanoparticulate exposure. Environ Sci Processes Impacts 15(1):49–62
29. Kuhlbusch T, Asbach C, Fissan H, Gohler D, Stintz M (2011) Nanoparticle exposure at nanotechnology workplaces: a review. Particle and Fibre Toxicology 8 (22):provisional version
30. Brouwer DH, van Duuren-Stuurman B, Berges M, Bard D, Jankowska E, Moehlmann C, Pelzer J, Mark D (2013) Workplace air measurements and likelihood of exposure to manufactured nano-objects, agglomerates, and aggregates. J Nanoparticle Res 15(11):1–14
31. Lee JH, Ahn K, Kim SM, Jeon KS, Lee JS, Yu IJ (2012) Continuous 3-day exposure assessment of workplace manufacturing silver nanoparticles. J Nanoparticle Res 14(9):1–10
32. Price HD, Stahlmecke B, Arthur R, Kaminski H, Lindermann J, Däuber E, Asbach C, Kuhlbusch TAJ, BéruBé KA, Jones TP (2014) Comparison of instruments for particle number size distribution measurements in air quality monitoring. J Aerosol Sci 76:48–55. doi:10.1016/j.jaerosci.2014.05.001
33. Zimmerman N, Godri Pollitt KJ, Jeong C-H, Wang JM, Jung T, Cooper JM, Wallace JS, Evans GJ (2014) Comparison of three nanoparticle sizing instruments: the influence of particle morphology. Atmos Environ 86:140–147. doi:10.1016/j.atmosenv.2013.12.023
34. Wang J, Asbach C, Fissan H, Hülser T, Kaminski H, Kuhlbusch TJ, Pui DH (2012) Emission measurement and safety assessment for the production process of silicon nanoparticles in a pilot-scale facility. J Nanoparticle Res 14(4):1–9. doi:10.1007/s11051-012-0759-y
35. Ji JH, Kim JB, Lee G, Bae G-N (2015) Nanomaterial release characteristics in a single-walled carbon nanotube manufacturing workplace. J Nanoparticle Res 17(2):1–18
36. Tsai C-J, Huang C-Y, Chen S-C, Ho C-E, Huang C-H, Chen S-W, Chang C-P, Tsai S-J, Ellenbecker MJ (2011) Exposure assessment of nano-sized and respirable particles at different workplaces. J Nanoparticle Res 13:4161–4172
37. Görner P, Simon X, Bémer D, Lidén G (2012) Workplace aerosol mass concentration measurement using optical particle counters. J Environ Monit 14(2):420–428
38. Kero I, Naess MK, Tranell G (2015) Particle size distributions of particulate emissions from the ferroalloy industry evaluated by electrical low pressure impactor (ELPI). J Occup Environ Hyg 12(1):37–44
39. Lanki T, Tikkanen J, Janka K, Taimisto P, Lehtimäki M (2011) An electrical sensor for long-term monitoring of ultrafine particles in workplaces. In: Journal of Physics: Conference Series, 2011. IOP Publishing, p 012013
40. Kim B, Lee JS, Choi B-S, Park S-Y, Yoon J-H, Kim H (2013) Ultrafine particle characteristics in a rubber manufacturing factory. Ann Occup Hyg 57(6):728–739
41. Li L, Zuo Z, Japuntich DA, Pui DY (2012) Evaluation of filter media for particle number, surface area and mass penetrations. Ann Occup Hyg 56(5):581–594
42. Tsai C-J, Liu C-N, Hung S-M, Chen S-C, Uang S-N, Cheng Y-S, Zhou Y (2012) Novel active personal nanoparticle sampler for the exposure assessment of nanoparticles in workplaces. Environ Sci Technol 46(8):4546–4552
43. Zhang M, Jian L, Bin P, Xing M, Lou J, Cong L, Zou H (2013) Workplace exposure to nanoparticles from gas metal arc welding process. J Nanoparticle Res 15(11):1–14
44. Chen S-C, Wang J, Fissan H, Pui DY (2013) Use of Nuclepore filters for ambient and workplace nanoparticle exposure assessment—spherical particles. Atmos Environ 77:385–393
45. Methner M, Hodson L, Dames A, Geraci C (2009) Nanoparticle emission assessment technique (NEAT) for the identification and measurement of potential inhalation exposure to

engineered nanomaterials—part B: results from 12 field studies. J Occup Environ Hyg 7 (3):163–176. doi:10.1080/15459620903508066

46. BSI (2010) (BSI PD 6699-3:2010) Nanotechnologies—Part 3: guide to assessing airborne exposure in occupational settings relevant to nanomaterials. British Standards Institution, London
47. Reuter M, et al. (2011) Approach towards an exposure assessment strategy for aerosols released from engineered nanomaterials from workplace operations. Paper presented at the INRS Occupational Health Research Conference, Book of Abstracts, Vandoeuvre, France
48. Koponen IK, Jensen KA, Schneider T (2010) Comparison of dust released from sanding conventional and nanoparticle-doped wall and wood coatings. J Expo Sci Environ Epidemiol 21(4):408–418
49. Brouwer D (2010) Exposure to manufactured nanoparticles in different workplaces. Toxicology 269(2–3):120-127. doi:10.1016/j.tox.2009.11.017
50. Brouwer D, Duuren-Stuurman B, Berges M, Jankowska E, Bard D, Mark D (2009) From workplace air measurement results toward estimates of exposure? Development of a strategy to assess exposure to manufactured nano-objects. J Nanoparticle Res 11(8):1867–1881. doi:10.1007/s11051-009-9772-1
51. Wang Y-F, Tsai P-J, Chen C-W, Chen D-A, Hsu A (2010) Using a modified electrical aerosol detector to predict nanoparticle exposures to different regions on the respiratory tract for workers in a carbon black manufacturing industry. Environ Sci Technol 44(17):6767–6774
52. Peters T, Elzey S, Johnson R, Park H, Grassian V, Maher T, O'Shaugnessy P (2009) Airborne monitoring to distinguish engineered nanomaterials from incidental particles for environmental health and safety. J Occup Environ Hyg 6:73–81
53. Dahm MM, Evans DE, Schubauer-Berigan MK, Birch ME, Deddens JA (2013) Occupational exposure assessment in carbon nanotube and nanofiber primary and secondary manufacturers: mobile direct-reading sampling. Ann Occup Hyg 57(3):328–344. doi:10.1093/annhyg/mes079
54. Shepard MN, Brenner S (2014) An occupational exposure assessment for engineered nanoparticles used in semiconductor fabrication. Ann Occup Hyg 58(2):251–265. doi:10.1093/annhyg/met064
55. Hedmer M, Isaxon C, Nilsson PT, Ludvigsson L, Messing ME, Genberg J, Skaug V, Bohgard M, Tinnerberg H, Pagels JH (2014) Exposure and emission measurements during production, purification, and functionalization of arc-discharge-produced multi-walled carbon nanotubes. Ann Occup Hyg 58(3):355–379. doi:10.1093/annhyg/met072
56. Schlagenhauf L, Chu BTT, Buha J, Nüesch F, Wang J (2012) Release of carbon nanotubes from an epoxy-based nanocomposite during an abrasion process. Environ Sci Technol 46 (13):7366–7372. doi:10.1021/es300320y
57. Xing M, Zou H, Gao X, Chang B, Tang S, Zhang M (2015) Workplace exposure to airborne alumina nanoparticles associated with separation and packaging processes in a pilot factory. Environ Sci Processes Impacts 17(3):656–666
58. Bello D, Wardle B, Yamamoto N, Guzman deVilloria R, Garcia E, Hart A, Ahn K, Ellenbecker M, Hallock M (2009) Exposure to nanoscale particles and fibers during machining of hybrid advanced composites containing carbon nanotubes. J Nanoparticle Res 11 (1):231–249. doi:10.1007/s11051-008-9499-4
59. Fonseca AS, Viitanen A-K, Koivisto AJ, Kangas A, Huhtiniemi M, Hussein T, Vanhala E, Viana M, Querol X, Hämeri K (2014) Characterization of exposure to carbon nanotubes in an industrial setting. Ann Occup Hyg. doi:10.1093/annhyg/meu110
60. Brouwer D, Berges M, Virji MA, Fransman W, Bello D, Hodson L, Gabriel S, Tielemans E (2012) Harmonization of measurement strategies for exposure to manufactured nano-objects; report of a workshop. Ann Occup Hyg 56(1):1–9. doi:10.1093/annhyg/mer099
61. Smith TJ, Kriebel D (2010) A biologic approach to environmental assessment and epidemiology. Oxford University Press, Oxford
62. Carrasco JL, King TS, Chinchilli VM (2009) The concordance correlation coefficient for repeated measures estimated by variance components. J Biopharm Stat 19(1):90–105

63. Pfefferkorn FE, Bello D, Haddad G, Park J-Y, Powell M, Mccarthy J, Bunker KL, Fehrenbacher A, Jeon Y, Virji MA, Gruetzmacher G, Hoover MD (2010) Characterization of exposures to airborne nanoscale particles during friction stir welding of aluminum. Ann Occup Hyg 54(5):486–503. doi:10.1093/annhyg/meq037
64. Sutariya VB, Pathak Y (2014) Biointeractions of nanomaterials. Taylor & Francis Group, Boca Raton
65. Plog BA, Quinlan PJ, Villarreal J (2012) Fundamentals of industrial hygiene. 6th edn. National Safety Council Press
66. Aldrich R, Arena L (2013) Evaluating ventilation systems for existing homes. Consortium for Advanced Residential Buildings, Norwalk. doi:10.2172/1064546
67. Hussein T, Kulmala M (2008) Indoor aerosol modeling: basic principles and practical applications. Water Air Soil Pollut Focus 8(1):23–34. doi:10.1007/s11267-007-9134-x
68. Hussein T, Korhonen H, Herrmann E, Hämeri K, Lehtinen KEJ, Kulmala M (2005) Emission rates due to indoor activities: indoor aerosol model development, evaluation, and applications. Aerosol Sci Technol 39(11):1111–1127. doi:10.1080/02786820500421513

Nanoparticle Release in Indoor Workplaces: Emission Sources, Release Determinants and Release Categories Based on Workplace Measurements

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Abstract Materials with one or more dimensions at nanosized scale have different properties from their larger physical forms; thus, they may interact differently with environmental and biological systems. However, the traditional risk assessment methodology (release/exposure assessment, hazard identification, hazard and risk characterisation) is not yet fully understood or has clear guidelines about the appropriate testing procedure for nanoparticles. Although exposure to NPs is being more widely characterised, mechanisms to determine the likelihood of release and transport of NPs in the workplace are still very scarce. Four main sources or domains for release have been identified: punctual or fugitive emissions, handling of bulk material at low energy, dispersion of highly concentrated NPs or application of end products with low concentration on NPs and abrasion or fracturing activities (high energy). To determine the release of NPs, an understanding of the release potential, appropriate metrics and measurement strategies and adequate instrumentation and identification of the potential sources of emission are fundamental. Several studies try to establish a methodology; thus, thorough review and intercomparison have been accomplished. Also, data retrieved from field measurements were analysed, showing that particle concentrations at 250 nm increased compared to background particles, occurring episodes of elevated particle number concentrations below 100 nm, although it was not clear whether this was associated with handling of and/or mixing operations or external sources to the process.

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1 Introduction

The use of engineered nanoparticles (ENPs) is growing continuously due to the increasing number of applications of nanotechnology, promoting the development of a new generation of smart and innovative products and processes that have created tremendous growth potential for a large number of industrial sectors [1].

Due to its potential to develop new added-value products, a staggering number of ENPs are already available on the market; however, along with the benefits, there is an ongoing debate about their potential effects on the human health or the environment. The uncertainties are extensive since it is now well established that engineered nanoparticles exhibit unique physical and chemical properties different from those of the same material in bulk form [2], affecting their physicochemical and biological behaviour, which can lead to adverse effects to both humans and the environment.

For a comprehensive risk assessment of ENPs, information is needed with respect to the intrinsic harmfulness of the particle (hazards), likelihood of exposure in a specific compartment (i.e. workplace, freshwater, marine water, sediments or soils, sewage treatment plant and air) and dose-response data (i.e. DNEL, derived no-effect level, PNEC, predicted no-effect concentration). Major investments have been done so far on the characterisation of the toxicological profile of the first generation of ENPs, including data on relevant human health endpoints such as acute toxicity, irritation and corrosivity, sensitisation, repeated dose toxicity, mutagenicity, carcinogenicity and reproductive toxicity, as well as data with respect to the nanoparticles' fate in the body (toxicokinetics, i.e. absorption, distribution, metabolism and excretion).

In contrast, research aiming to improve our understanding of the possible exposure arising from all stages of the production, use and disposal of nanoparticles is far less advanced. The amount of research activities focused on the evaluation of the likelihood of exposure has increased in the last decade in parallel with the increased interest of the industry on the production and use of ENPs for developing new added-value products. There are increasing concerns over possible human health risk associated with the use of ENP as far as the production volumes of some ENPs are already exceeding thousands of tonnes and that the global demand for ENPs is expected to exceed $3.1 trillion by 2020 [3], which directly implies an increase of the likelihood of the potential exposure to ENPs during production, use and end-of-life treatments in the near term.

Hence, in the coming years, a remarkable challenge for the nanotechnology industry, the academia and the regulators will be the generation of new data on the levels of exposure in workplaces. In the occupational context, it has been demonstrated that workers have the potential to be exposed to unique ENPs with novel sizes, shapes and chemical properties, at levels far exceeding ambient concentrations [4]. Recent studies show how the most extensive exposures to ENPs likely occur in the workplace, particularly research laboratories, start-up companies, pilot production facilities and operations where ENPs are processed, used, disposed or recycled [5].

The routes of exposure are also well characterised, being inhalation the most common route of exposure to airborne ENPs in the workplace. The skin has also been investigated; however, most studies have shown little to no transdermal ENP absorption [6]. Oral (gastrointestinal) exposure can occur at the workplace from intentional ingestion, from unintentional hand-to-mouth transfer, from inhaled particles >5 μm that are cleared via the mucociliary escalator and of drainage from the eye socket via the nasal cavity following ocular exposure [4].

Similarly, recent publications and reports arising from research activities conducted within the frame of the EU 7th Framework Programme (FP7) projects, such as GUIDEnano (FP7 GA no. 604387), NanoMICEX (FP7 GA no. 280713), Sanowork (FP7 GA no. 280716) or SCAFFOLD (FP7 GA no. 280535), have demonstrated the likelihood of exposure and release across the life cycle of common ENPs. Exposure measurement surveys conducted under the framework of these projects using real-time measurement devices to obtain particle number concentration (particles/cm^3) and mass concentrations (μg/cm^3) demonstrated that nanoparticles can be easily dispersed as a dust (e.g. powder) or an airborne spray or droplets, resulting in a potential exposure via inhalation or skin penetration.

So far, the evaluation of the exposure has been based on the explorative research of the levels of exposure in the worker's breathing zone and/or areas where the activities involving the production and use of ENPs take places. However, this trend has evolved over the last couple of years towards a more comprehensive research, where a clear understanding of the potential sources of release of nanoparticles in workplaces and the underlying mechanism and factors determining the transport and transformation process of the ENPs released in the workplace air are essential to understand the current levels of exposure to ENPs, with special emphasis on the characteristics of the ENPs when they reach a human receptor after transport over a distance from an ENP source [7].

Within this approach, the evaluation of the potential of exposure to nanoparticles in the workplace requires information at both source and receptor level. The likelihood of release is always the result of the combination of material properties and process/ activity parameters, while the potential of exposure is determined by a variety of factors affecting the behaviour of the nanoparticles released in the workplace, including the effect of coagulation, scavenging and surface deposition during the transport of ENPs from the source to the receptor, as well as the concentration and size mode of the emitted nanoparticles and background aerosols, source to receptor distance or ventilation characteristics, among other parameters [8].

The number of published data on the levels of exposure to ENPs in the workplace has increased substantially over the last five years. However, the amount of available data on the mechanisms that determine the likelihood of release and the transport of ENPs released in the workplace air is still very scarce. The conceptual model for assessment of inhalation exposure to ENPs published by Schneider et al. [8] in 2011 is a backbone study in this field that reflects the importance of a proper release characterisation when assessing the exposure to ENPs, as well as the role of coagulation, scavenging and surface deposition on particles emitted during synthesis, downstream use and application or treatment of products containing embedded ENPs. This study defines *four source domains* based on current and near-future exposure situations for ENPs. Each source domain reflects different mechanisms of release and therefore different forms of released ENPs.

This conceptual model assumes that the form and amount of ENPs released are determined by the activity emission potential and the substance emission potential. Both variables are essential when assessing exposure to ENPs. The activity emission potential is commonly related with the amount of products (i.e. ENPs or nanoproducts) used, energy applied in the process and level of containment. The substance emission potential can be considered specific of each ENP or nanoproduct. For ENPs in powder form, the emission potential will be determined by the dustiness of the material. In the case of colloidal dispersions containing ENPs, the concentration of the solute, diameter of dispersed ENPs and viscosity of the mixture are key parameters influencing the emission potential [9].

This chapter includes a complete analysis of the characteristics of the most relevant sources of airborne nanoparticles associated with the life cycle stages of ENPs, including production of ENPs by relevant synthesis approaches, downstream use in relevant sectors, incorporation of ENPs in a matrix as well as activities related to end-of-life treatments.

Understanding release potential is an important starting point towards an accurate understanding of the exposure potential of workers. However, while ENPs' release is a prerequisite of downstream exposure, very little attention has focused on understanding the potential and conditions for release of ENPs in workplaces. According to the strategic research agenda on nanosafety in Europe published in 2013 [1], research and development activities aimed at understanding processes relating with release are likely to increase in the near future since this allows a proper understanding of the nature and extent of the exposure in those areas of possible release of ENPs.

A number of studies that focused on the evaluation of the release of ENPs in workplace environments have been published to date, and this chapter will give an update of the existing publications in this field.

The last but not the least important aspect to be considered when assessing the exposure to ENPs is the selection of appropriate metrics and measurement strategies to quantify the levels of release and/or exposure in the workplace. Particle number concentrations and particle number size distributions are the most commonly used metrics; however, there is a lack of international consensus about which measurement parameters (solubility, size, surface area, morphology, composition, degree of agglomeration/aggregation, surface modifications or reactivity, number concentration and/or mass) provide the most reliable metrics [10].

In relation to the measurement strategies, several approaches to achieve a quantitative assessment have been proposed and discussed by relevant organisations such as the US National Institute for Occupational Safety and Health (NIOSH) or the Partnership for European Research in Occupational Safety and Health (PEROSH). These strategies are based on the application of a tiered approach where information is collected in each successive tier at a more detailed level in order to reduce the uncertainty in the measurements.

A number of approaches have been published to date [11–13], being a key priority within the nanosafety research community. All of them are based on four main steps, including (1) identification of the potential sources of emission (e.g. dedicated questionnaires); (2) definition of the measurement strategy, including instrumentation and metrics; (3) evaluation and characterisation of the background levels of ENPs, describing sources of ENPs and characteristics, and (4) data processing.

The development of adequate instrumentation has been paid much attention in the last few years, including portable and non-portable instruments that monitor ENPs in quasi-real time and instruments that sample (time-aggregated) ENPs on a substrate, followed by off-line analysis using techniques such as inductively coupled plasma mass spectrometry (ICP-MS), energy-dispersive X-ray fluorescence (ED-XRF), atomic force microscopy (AFM), electron microscopy (EM) and X-ray diffraction (XRD).

A suite of real-time devices are already available, and new devices are likely to become available on the market in the near future. The most employed devices include portable condensation particle counters (CPCs) in the size range of 10 to 1,000 nm, portable optical particle sizers (OPS) in the size range of 0.3 to 10 μm, transportable surface area monitors in the size range of 10 to 1,000 nm and high-sensibility particle sizers depending on the time resolution needed such as the

SMPS, scanning mobility particle sizer (<30 s), or the FMPS, fast mobility particle sizer (1 s).

The combined use of these instruments will provide valuable information on the levels of release and exposure to ENPs, including particle number concentration (particles/cm^3), size distribution and surface area (μm^2/cm^3), all relevant metrics for risk assessment.

Apart from the direct-reading instruments, the collection of air samples in adequate filter media is necessary to determine the chemical composition of the airborne ENPs. To this end, appropriate air sampling filter media must be selected depending on the type of ENM and desired analytical information. In this sense, traditional open-faced cassettes (37 mm) are used.

This chapter provides a complete review of the current knowledge on the sources and determinants of release, both key parameters on the evaluation of the likelihood of exposure in the workplace. Moreover, a comprehensive review of the existing publications on ENPs' release have been conducted to define the nature and extent of ENPs' releases in workplace environments and to categorise such releases in well-defined ENP release categories based on the activity emission potential of ENPs and the characteristics of the compartments through which the ENPs may pass during their transport from the source to the receptor.

We also present new data extracted from the FP7 project NanoMICEX, where a complete analysis of the levels of release and exposure during the manufacturing and downstream use of ENPs in the pigment and ink sector was conducted.

2 Sources of Nanoparticles in Workplaces

The increased production of ENPs may lead to an increased concentration of these materials in the workplace. ENPs are emitted by a broad spectrum of potential sources that can be classified according to different criteria such as the origin (i.e. natural, accidental or anthropogenic) or the activities resulting in the release (e.g. fugitive emissions, handling and transfer of bulk ENPs, mixing operations and/or abrasion of nanoproducts).

According to the origin, nanoparticle aerosols in workplaces can be classified as engineered nanoparticles (ENPs), incidental or process-generated nanoparticles (PGNP) and background aerosols (BA).

The background nanoaerosols' (BA) concentration originates from natural sources and anthropogenic activities like combustion [14]. Natural sources of nanoparticles in the atmosphere include volcanic eruptions, physical and chemical weathering of rocks, precipitation reactions and biological processes [15]. Anthropogenic sources include industrial- and domestic-related sources. Industrial sources are predominately from combustion processes, whereas domestic sources can be from simple tasks such as cooking. Vehicle sources are also of prime importance, being currently the most studied and considering both non-exhaust emissions from tyres and brakes and direct emissions from the combustion of the different types of fuel used.

The concentration levels of BA in occupational environment vary depending on the containment of the sites and/or processes [7]. In case of a clean-room environment, the concentration of BA is much lower than NPs released from the activities involving the handling and use of ENPs. In contrast, in workplaces where BA from ambient are likely to be present, the concentration of BA can be in similar range to or even higher than ENPs emitted. Commonly reported concentrations of BA in workplaces are in the range of 10,000 to 20,000 NPs/cm^3 [15, 16].

Process-generated nanoparticles (PGNP) include combustion-derived nanoparticles (CDNP) and engine-generated nanoparticles (EGNP). CDNP present a diverse group of particles which gain commonality because of their origin in combustion processes. Like other nanoparticles, CDNP show a considerable heterogeneity in composition [17]. On the other hand, EGNP present at workplaces may be generated, for example, by electrical equipment like compressors, universal motors, drilling machines and vacuum cleaners and by diesel engines [18, 19]. Measurements suggested that workplace concentrations due to EGNP emissions may exceed several 100,000 NPs/cm^3 up to several million NPs/cm^3 [14, 18].

Exposure to PGNP has been reported in a number of studies published recently [20–24]. PGNP have been reported in number concentrations exceeding 10^4–10^6 ENPs/cm^3. For risk assessment and management, PGNP and background aerosols shall be distinguished from the actual exposure to engineered nanoparticles [25].

Much of the nanoparticles present in the workplace environment can be classified according to some of these categories. The sources of nanoparticles have been defined in several studies [8, 26], highlighting the so-called source domains proposed by Schneider et al. [8]. These source domains reflect the vast majority of current and near-future exposure situations of nanoparticles and nanoproducts. The proposed source domains reflect different mechanisms of release and consequently possible different forms of released aerosols. Moreover, they are associated with the life cycle stages of the nanoparticles.

Seipenbusch [26] proposed also a way of classifying the sources of nanoparticles in the workplace by following the process chain in production and application. The author distinguishes three main types of sources, including primary, secondary and tertiary nanoparticle aerosol sources. Primary nanoparticle aerosol sources may occur due to leakage from a synthesis process or welding operation, potentially releasing large quantities of nanoparticles into a workplace environment [27, 28]. This source typically leads to a continuous particle release over a long period of time.

Secondary nanoparticle aerosol sources are mainly due to processes such as bagging, emptying or dumping. Much of the workplaces studies conducted so far are related with this source. These studies do not show a significant concentration of nanoparticles in workplace air. Even for the production of commodity nanopowders on the large scale, such as SiO_2 or ZnO, handling and bagging of powders apparently do not lead to the emission of nanoparticles into the workplace environment. The study conducted by Kuhlbusch et al. in 2011 [29] summarises a number of workplace processes investigated in the past decade, reporting releases of airborne nanoparticles in processes such as weighing, mixing, pouring and transferring, leading to possible exposure. Release potential may be higher when conveying or drying products, during reactor maintenance and cleaning and during material-handling task [30, 31].

Finally, a tertiary nanoparticle aerosol source may originate from the use or processing of products or intermediates containing nanoparticles. Examples of this source are spraying of particulate suspensions or the compounding of nanopowders with polymers [32]. The likelihood of release of the original particles is extremely low according to recent studies. Therefore, large matrix-bound particles are expected.

The classification of the sources proposed by Schneider et al. has gained momentum in recent years. The four source domains defined by this author are associated with the life cycle stages of the nanoparticles, from production, downstream use, to end-of-life treatments and include:

1. Point source or fugitive emissions
2. Handling and transfer of bulk manufactured nanomaterial powders with relatively low energy
3. Dispersion of either (liquid) intermediates containing highly concentrated ($>25\%$) nanoparticles or application of (relatively low concentrated $< 5\%$) ready-to-use products
4. Activities resulting in fracturing and abrasion of manufactured nanoparticle-enabled end products at worksites such as abrasion, manual sanding, grinding, drilling or cutting

The first source domain considers the release of nanoparticles during the production phase (synthesis) before harvesting the bulk material. Examples under this source domain include emissions from a reactor during a flame spray pyrolysis synthesis, leaks through seals and connections and incidental releases. The types of nanoparticles released during this process include both process-generated nanoparticles (PGNP) and engineered nanoparticles.

The second source domain includes activities related with the production of nanoparticles and downstream processes including using nanoparticles for the manufacturing of nano-enabled products. Examples of such activities include the collection and harvesting of ENPs, packing or weighting, among other activities. In this source domain, much of the nanoparticles emitted can be classified as engineered nanoparticles.

The third source domain includes activities related with the preparation of highly concentrated ($>25\%$) nanoparticles dispersions or the application of products containing relatively low concentrations of nanoparticles ($<5\%$) such as nano-enabled products for personal care, for example, spraying of personal care products that can generate large fractions of aerosols in the nanometre range after condensation.

Finally, the fourth domain includes activities related with mechanical processes that may lead to the liberation of nanoparticles from a matrix. As stated previously, nanoparticles embedded in a solid matrix are unlikely to be released during handling, although it is possible that if the matrix is subject to high mechanical and thermal energies, such as when being cut or ground, nanoaerosols may be released [33]. However, the number of research efforts that deliberately investigate release from a solid is still scarce. The particulate material released is most often a mixture of multiple elements, including particles of matrix alone, particles of matrix with the nanomaterial embedded, as well as nanoparticles fully dissociated from the matrix [34].

Studies conducted by the nanosafety research group of ITENE under the framework of the NanoSafePack project revealed that a significant release of submicron-sized particles, including both inhalable (10–4 μm diameter) and respirable (<4 μm diameter) particles, can be expected during sanding and drilling processes of polymer-based nanocomposites, where a high energy level is applied. The milling process generates fragments of both polymer-containing nanoparticles and polymer alone, typically aggregated due to warming of the polymer during the milling. Finally, the cutting and sawing process generates a nonsignificant level of release due to the low-energy level applied.

A summary of relevant sources of nanoparticles in the workplace are listed in Table 1. Moreover, data on particle size distribution and typical concentration ranges extracted from peer-reviewed publications are included in the table.

The exposure to ENPs in the workplace will depend on the type and characteristics of the source, as well as on the processes altering the properties of the nanoaerosol during the transport from the source to the receptor (i.e. particle breathing zone). Understanding the link between release, transport and exposure is therefore essential for risk assessment purposes.

Current data on the determinants of release and mechanisms related with the changes in the particle characteristics during the transports of the nanoaerosols from source to receptor will be discussed under the following chapters.

3 Determinants of Release: Emission Potential, Activity Emission Potential and Controls

Characterising the release of airborne nanoparticles during synthesis, downstream use, application or treatment of products containing embedded ENPs has always been a subject of interest in workplace air quality measurements. A number of research activities aiming to answer the question whether airborne particles could be released from a particular activity during the life cycle of the material have been conducted so far. However, a lack of understanding still exists on the mechanism that governs the release of nanoparticles in occupational environments, and no significant attempt has been made to verify the existence of a generalisable trend in the release of nanoparticles from a nanotechnology process [50].

Table 1 Examples of emission sources and types of released nanoparticles

Emission source	ENPs' release potential	NPs' type	Measured level range	References
Primary/SD1				
Liquid-phase reaction	Likely	PGNP	4.0×10^4 to 11.0×10^6	[35]
Flame spraying	Likely	PGNP	4.7×10^3 to 1.0×10^6	[36–38]
CVD	Not excluded	PGNP	Nonsignificant	[39]
Top down (milling)	Not excluded	ENPs/PGNP		
Secondary NP aerosol/SD2				
Weighing of powders	Likely	ENPs	2.0×10^4 to 7.0×10^4	[40]
Harvesting	Likely	ENPs	2.0×10^4 to 5.0×10^4	[40]
Manual packaging (bagging)	Likely	ENPs/PGNP	20.0×10^4	[41]
Bag emptying of powders	Likely	ENPs	Significant increase	[42, 43]
Melt blending	Likely	ENPs/PGNP	$>1.0 \times 10^5$	[32]
SD3a/SD3b				
Spraying of liquid	Very likely	ENPs	2.0×10^8	[44]
Spraying (gas)	Very likely	ENPs	1.6×10^5 to 2.0×10^{10}	[45, 46]
Injection moulding	Very likely	ENPs	$>8.0 \times 10^5$	[42]
Brushing and rolling	Very likely	ENPs	$>6.0 \times 10^5$	[29]
Sonication of nanodispersions	Very likely	ENPs	$>8.0 \times 10^6$	[28]
Tertiary NP aerosol/SD4				
Abrasion of nanoproducts	Not excluded	PM/EMNP	8.0×10^3 to 2.0×10^4	[47]
Drilling	Possible	PM/EMNP	4.0×10^4	[19]
Grinding	Possible	PM/EMNP	3.0×10^3 to 1.0×10^6	[48, 49]

PNC particle number concentration, *PSD* particle size distribution, *CVD* chemical vapour deposition

A better understanding of those mechanisms affecting the release or emission rate of ENPs at different life cycle stages is essential to understand the potential exposure to ENPs in occupational environments. It is now generally agreed that the main parameters determining release or emission rates are either the *inherent properties of the nanoparticles*, such as size, chemical composition and surface properties, and the *operational factors of the nanotechnology process* that the nanomaterials undergo.

The inherent properties determine the so-called substance emission potential (E), which describes the potential of the product to become airborne. For particulate agents, the potential to become airborne is dependent on dustiness. For liquids and liquid mixtures, the potential to become airborne is dependent on volatility, and parameters such as the concentration of solute, diameter of dispersed particles in liquid and viscosity. For powders, the emission potential is influenced by parameters such as particle size (distribution), aggregation, coalescence, cohesion, moistness of product and surface modifications, all of them properties influencing the dustiness of the material.

The operational factors influencing the potential of the activity to generate airborne nanoparticles constitute the *activity emission potential* (H), which is determined by the level, type and amount of energy applied, scale (e.g. amount of product used), product-to-air interface (e.g. level of containment), frequency and duration of activities (duration per task/activity).

Besides substance and activity emission potential, there are other relevant factors that may have an effect on the release potential of ENPs, including geographical location, rate/volume of production, work practices and work environment factors such as temperature or indoor humidity.

3.1 Role of the Activity Emission Potential in the Release of NPs in the Indoor Environment

The activity emission potential (H) is directly related with the operational conditions implemented in the workplace during the production and downstream use of ENPs and/or nanoproducts. The main operational conditions related with the emission potential include duration and frequency of exposure, applied amount of ENPs, temperature, containment of the process and capacity of surroundings. Moreover, the specific risk management measures (RMM) and good industrial hygiene practices implemented to minimise exposure of workers during and after normal operations are also essential in the activity emission potential.

An overview of these parameters and specific issues related with the use of ENPs in occupational settings is provided within Table 2.

The level and type of energy applied is a key underlying determinant of release, being directly related with the source strength. Hence, a better understanding of this modifying factor is essential to estimate the release of ENPs in the indoor

Table 2 Main release-modifying factor in occupational environments

Release-modifying factor	Description	Nano-specific issues
Duration and frequency of exposure	Describes the duration and frequency of those activities involving a potential release of ENPs in the life cycle, from production and downstream use, production of nanoproducts, to end-of-life treatments	It is recommended the use of the realistic worst-case combination of duration and frequency of use for one worker
Applied amount of ENPs	Describes the maximum amount of ENPs used in a determined scenario. In some situations, however, the exposure is related to certain activities (e.g. maintenance and cleaning) more than to the amount handled	The amount of ENPs is generally low. It is recommended to refer the study to the maximum realistic amount of ENPs used
Temperature	Describes the temperature of the process. With respect to exposure, the most important issue is that volatility is dependent on temperature. This mainly affects release from liquid dispersions	The most important issue is the effect of the temperature on the formation of ENPs from volatile drops generated after the evaporation of nanofluids
Containment of the process	Describes the level of containment of the process. The level and means of containment determine the release potential (e.g. closed process equipment/glove box can reach up to 100% of containment)	Limited information on the effectiveness level of conventional containment systems against ENPs
Capacity of surroundings	Describes the characteristics of the area where the activity takes place. Room volume and ventilation have a direct impact on the concentration and dilution of background aerosols in the air	The concentration of background aerosols is essential in the transport and transformation process of ENPs once released
RMMs and industrial hygiene practices	Describe the specific types of controls applied on site to limit the release of ENPs, including the use of engineering controls aimed at reducing the release of NPs from specific sources. The use of localised controls in the close proximity of the source is essential	Good hygiene practices such as cleaning limit the release of deposited ENPs due to natural means or general workplace activities
Energy applied to the process	Describes the type and level of force applied under normal operational conditions, including motive forces, gravitational, friction, heat, pressure drop and other dispersion forces	Pressure drop and frictional forces are of special interest in indoor environments, causing intentional or unintentional release of ENPs
Physical form of the product	Describe the physical state of the ENPs under conventional operations, including powder forms, liquid dispersion and particle-matrix complexes	Dustiness in powders and concentration of ENPs in liquid are key parameters influencing the release potential

environment. In essence, the type of energy applied can be divided into five main classes, including motive forces, gravitational and impaction forces, friction, pressure drop and other dispersion forces and heat.

Motive forces are primarily related to movement of product or movement of objects contaminated with a product. It excludes motion where friction is caused between bound materials. Gravitational and impaction forces are primarily related to forces during falling and caused by the final impact on surfaces. These three forces are relevant for fugitive emissions in several life cycle stages, including production and downstream use of ENPs.

Frictional forces are primarily caused during an activity where friction between bound materials and collisions induced by friction cause comminution. These forces are considered to be important during operations such as abrasion or drilling within the fourth source domain described previously.

Pressure drop and other dispersion forces such as spraying are primarily caused by pressurised sources or other forces/techniques causing intentional or unintentional dispersions of ENPs into the air. These forces are relevant in activities such as the application of dispersions of ENPs using hand-spray bottles or pressurised cans.

Finally, there is also evidence that heat modifies the exposure in workplaces. Heat energy may be actively applied during the process, or it may also present as a result of a chemical reaction process. This last force is generally determined by, e.g. processing temperature (melted solids), voltage or agitation level.

The scale of the activity is relevant in terms of emission potential of bulk materials; however, the influence in the context of ENPs is expected to be limited due to the current production levels. This parameter is commonly expressed in terms of application rate (kg or l/h), amount produced or volume of materials processed per time unit (m^3/h).

Other factors reported by different authors [9, 51, 52] that may affect the release potential in occupational environments are the following:

- Localised controls: risk control measures in close proximity of the source intended to remove emissions (such as local exhaustive ventilation or wet suppression techniques).
- Segregation: isolation of sources from the work environment without containment of the source itself (e.g. with a separated drying room).
- Separation: referred to providing a worker with a personal enclosure within a work environment (e.g. air-conditioned cabin) and also referred to contain the source for remove emissions (e.g. with a glove box).
- Dispersion (dilution): outdoor/indoor work, using natural and mechanical ventilation, which determines the dilution of air contaminants through the room. Room size, changes per hour, etc. are dispersion factors affecting exposure.
- Organisational measures: hygienic and safe work protocols in place, training, supervision, etc.
- Worker behaviour: hygienic and safe practices (cleaning hands, using EPIs, following workplace protocols, etc.).

- Surface contamination and fugitive emissions: emission related to release of deposited contaminants on surrounding surfaces (including worker clothing) due to natural means or general workplace activities (e.g. moving equipment/vehicles) and unintended and unpredictable leaks from process equipment. Room size and general ventilation strongly influence dispersion of airborne nanomaterials. For large rooms and high general ventilation rates, the duration of the activity made little difference to dispersion but not for small poorly ventilated rooms [13]. Regarding such factor, effectiveness of housekeeping practices is of great importance.
- Conditions and measures related to personal protection and health evaluation: personal protection (gloves, face protection, full-body dermal protection, goggles, respirator, etc.), correct replacement, cleaning and maintenance of RMMs, etc.

It should be noted that much of the factors described previously can be influenced by personal behaviour and skills of the individual worker. The way the nanoparticle is handled or the performance of activities such as mixing or stirring may be very prone to behaviour, with a direct impact on the release potential of the activity.

3.2 Substance Emission Potential: Physical Form of ENPs and Nanoproduct Specifications

The physical form of the product is a key factor for the emission potential of ENPs in the indoor environment. For powders, the emission potential is determined by the dustiness of the material handled, understood as the intrinsic potential of a determined ENP to become airborne. The powder form may be supplied as fine powders (high dustiness), agglomerated powders (medium dustiness) and pellet-type solids (low dustiness). Much of the ENPs in powder form can be assigned to one of these powder categories, covering fine dust and/or extremely dusty forms. These categories are also applied in relevant exposure estimation models for risk assessment purposes such as ART [53] or Stoffenmanager [54].

Several parameters will influence the mass of the dust liberated from an ENP being handled, including the amount and type of energy applied in the process, time frame of the working procedure, moisture content of the powder or air humidity during the handling and electrostatic and surface properties of the powder.

In case of a liquid, liquid dispersions may form aerosols or splashes when processed under input of mechanical energy. Key parameters related to the emission potential in liquid dispersions include: the concentration of the solute, diameter of dispersed particles and viscosity [9]. However, processed in low-energy processes and under good industrial hygiene conditions, release from charging, discharging and processing is mainly driven by vapour pressure and water solubility

For articles containing nanoparticles, the ratio of surface to volume is a key driver for the fraction of substance that may be released into the environment or is available for direct exposure of humans (oral or skin contact). Similarly, the product specifications, i.e. concentration/percentage of the nanoparticles in a mixture or article, may be directly linked to the release rate of ENPs in workplace environments.

The matrix material is a stronger determinant of the size distribution of the ENPs emitted during the handling of liquid dispersions or articles, whereas the concentration of ENPs may affect the amount of ENPs generated.

3.3 Current Knowledge in the Release of NPs in the Indoor Environment

The enormous variability in the properties affecting the substance emission potential (E) when considering nanoparticles, together with the current lack of information on the existing operational conditions, makes difficult the establishment of a clear particle release patter from a particular activity. A clear understanding of such relationships is essential to define the specific determinants of releases and, therefore, the main parameters to be considered to ensure a high level of protection of human health and the environment from the risks that can be posed by ENPs in occupational environments.

To this end, new studies will be needed to define variations in the release of ENPs caused by parameters directly related with the substance and activity emission potential, including particle size, surface chemistry, concentration/percentage of the ENPs in a mixture or article, duration of the activity, process temperature, containment of a process and any specific operational conditions, among others parameters.

Several studies have been conducted so far, including different types of ENPs and nano-enabled products and processes. Metal and metal oxides, together with carbonaceous nanoparticles, are the most studied [35, 55–57]. Among the nanoproducts currently in the market, several studies that focused on the evaluation of the potential release of nanoparticles from polymer-based nanocomposites and nano-coatings have been published in the past 5 years [39, 58, 59].

Almost all of the existing studies in the area show a clear evidence of release of nanosized structures, including ENPs as such or embedded into a solid matrix. In relation to the use of ENPs in the composite industry, several studies show a substantial release of nanoparticles (NPs) during the production process [49, 60, 61].

The review of existing research on the release of nanoparticles from solid nanocomposites conducted by Frogget et al. in 2014 [34] identified 54 studies that specifically investigated the release of nanoparticles under different operational conditions, including machining, weathering, washing, contact and incineration.

This study showed that nanostructured materials were frequently released from nearly all of the nanocomposites and base matrices examined. The results show that the release of dissociated ENPs was only detected in 31 % of the studies in which release occurred, which implies that while degradation occurs, ENPs often remain tightly bound to the matrix.

Another relevant study concerning release in workplace environments was conducted by Vance et al. in 2015 [62]. This study analysed 31 references, published over the last 7 years, which investigated the release of aerosols from use and wear and tear of products enhanced with engineered nanomaterials. Moreover, the authors conducted a thorough study of the types of nanotechnology-enhanced consumer products that have the greatest potential to aerosolise engineered nanomaterials into indoor environments, such as homes, office buildings, schools, hotels and hospitals.

Many of the products described within this study can be used in workplaces or in outdoor environments by professional workers. These products include composites, paints, coatings and sprays (using manual pumps or in pressurised cans), among others. Despite the scarcity of published information on the release potential of ENPs from these types of products, it is evident that the use of commercial spray dispensers can generate water droplets with embedded nanoparticles. Similarly, several studies have reported dust emissions from paints and coatings enhanced with ENP [61].

These studies do not provide insights into the factors determining the release of ENPs in occupational settings; however, a thorough evaluation of the data reported within existing publications can provide a better understanding of mechanisms leading to the release of ENPs in the workplace.

To date, it is clear that release during production and downstream processing of ENPs is expected to occur under typical conditions of use. However, the amount and physical characteristics of the resulting emissions are not clearly understood. We can expect that different release patterns may arise based on the method of ENP synthesis and products into which ENMs are incorporated, but given the lack of monitoring of industrial emissions of ENPs and scarce information on production processes, it would be difficult at this stage to account for such differences.

New studies based on experimental observations are urgently needed to improve the current understanding of the effects of the operational conditions on the release patters of ENPs. It is unlikely that a general rule can be developed for predicting the nature and extent of ENPs release; however, some general assumptions can be done.

Table 3 shows recent data on the emissions rates at different stages of the life cycle. The table includes information of the operational activities and forces involved in the release.

Besides the inherent properties of the ENPs and the activity emission potential, the presence of emission control devices has to be also considered to support a proper evaluation of the likelihood of release of ENPs in workplace environments. However, to date, there is considerable uncertainty on the amount of ENPs that may be removed by existing control devices.

Table 3 Examples of emission sources and main properties of released nanoparticles

Activity	Forces involved	Particle specifications
Handling of powders	Motive forces	Single particles and aggregates <1,000 nm
Spraying (pressurised)	Pressure difference	Single particles as well as large agglomerates Size range: nm to 20 μm
Spraying (hand-spray)	Pressure difference	Single particles as well as large agglomerates Size range: nm to 20 μm
Compounding of nanocomposites	Motive forces	Embedded particles. Limited release of fully dissociated NPs
Abrasion of nanoproducts	Frictional forces	
Sanding paints	Frictional forces	
Wet milling/cutting	Frictional forces	

The evidence for effectiveness of control measures such as local exhaust ventilation (LEV) systems and enclosures is very limited. Experimental studies conducted under recently finalised FP7 funded projects demonstrated that a proper hood design together with an adequate airflow is key to ensure the capture of much of the nanoparticles released to the workplace environment.

The effectiveness of filters to intercept ENPs is also an essential factor to support the evaluation of the potential release of ENP when the process is completely contained.

Finally, the behaviour of the workers will also affect the nature and extent of the release during the production and downstream use of ENPs. The establishment and implementation of working procedure designed to reduce and/or limit the release of ENPs to the workplace environments have gained attention in recent years.

4 Evaluation of the Potential Releases of Engineered Nanoparticles in the Workplace: Experiences from NanoMICEX

4.1 Overall View of the Project

NanoMICEX is a collaborative project funded by the European Union Seventh Framework Programme (FP7/2007–2013) under Grant Agreement no. 280713. The overall objective of the project is to develop an integrated strategy to ensure the safety of workers dealing with nanoparticles, with specific focus on developing standard techniques to obtain less hazardous and more stable NPs, assess the workers' exposure and provide cost-effective methodologies to protect workers and the environment from the release of nanoparticles during all stages of the nanotechnology-based ink and pigment production, use and disposal.

The activities related with the release and exposure assessment were coordinated by the exposure assessment research team of the Institute of Occupational Medicine (IOM), the leading organisation in this field. The activities conducted focused on the identification and quantification of the potential release of NPs at multiple stages of the life cycle, including synthesis, production of intermediate ENPs and formulation of products (directly from ENPs or from intermediates).

Within NanoMICEX, a thorough study of the potential release of ENPs in several industrial facilities was conducted. Related to the nanoparticles considered, NanoMICEX was focused on those nanoparticles employed in large scale by ink and pigment industries, covering an extensive range of high-tech applications and added-value properties (semiconductor, insulator, luminescent, catalytic, refractive and magnetic properties). Such criteria are satisfied by several metal oxide nanoparticles (ZnO, TiO_2, Al_2O_3 and Fe_3O_4), Ag metal nanoparticles, CdSe quantum dots and the mixed metal oxide cobalt aluminate spinel.

4.2 Scope of the Studies Conducted

Exposure and release assessments were carried out at five companies involved in the manufacture and downstream use of ENPs in the pigment and ink sector using a tiered approach. This approach is based on tier 1 scoping visit focused on the compilation of contextual information on the operative conditions and risk controls applied, including a first analysis of the particle number concentration using hand-held instruments such as particle counters and optical particle sizers, and a tier 2 multi-instrument measurement survey to obtain a large amount of data on relevant metrics, including particle size distribution, surface area and mass.

The case studies conducted under the project and reported within this chapter include the following processes and activities:

1. Synthesis of nano-ZnO by flame spray pyrolysis/dry synthesis
2. Functionalisation of nano-ZnO
3. Preparation of a nano-enabled prototype paint from pristine nanopowders
4. Inkjet printing under controlled conditions

An overview of the activities monitored and relevant operational information for risk assessment purposes are provided in Table 4.

4.3 Methods, Devices and Measurement Strategies Applied

The methodology applied with NanoMICEX was based in a tiered approach, including a tier 1 study that focused on the identification of the sources of emission,

Table 4 Case studies conducted within NanoMICEX

Case study	Process operation	Operative conditions/RMMs	Contributing scenarios
Synthesis of nano-ZnO by flame spray pyrolysis	The synthesis process is conducted in a pilot plant area by spray pyrolysis. This process is a high-temperature gas-phase process for nanoparticle production, in which starting materials are liquid precursors containing the appropriate metal species for particle formation. These precursor solutions are metered to a spray nozzle where they are dispersed by a stream of oxygen and ignited with a methane flame Nanoparticle formation and growth takes place in the high-temperature zone of the flame, being the growth process controlled by the precursor concentration and the flame properties. Typically, product nanoparticles are collected with filters as a dry powder	Production rate: 1 kg h^{-1} Ventilation Air changes: on average 10 changes/day Active LEV in the room Containment: pyrolysis unit enclosed PPE: RPE and DPE	ES1. Pyrolysis reaction ES2. Harvesting
Functionalisation of nano-ZnO	The functionalisation of nano-ZnO involves treating a suspension of the nanoparticles with a reagent in order to functionalise the surface, isolating the functionalised nano-ZnO from the reaction mixture, drying and mixing them with a varnish. All tasks are largely carried out by hand (in the glove box, in the fume hood or in the sonicator) by two employees	Production rate: 1 l h^{-1} Ventilation: vertical air flow/0.30 m/s Containment: all processes are carried out in a glove box or fume hood PPE: RPE and DPE	ES1. Weighing, charging and mixing ES2. Functionalisation ES3. Packaging

(continued)

Table 4 (continued)

Case study	Process operation	Operative conditions/RMMs	Contributing scenarios
Preparation of a nano-enabled prototype paint from pristine nanopowders	Laboratory scale batch preparation of nano-enabled prototype paint from pristine nano-ZnO and nano-TiO2 powder The production of nanopaints involve weighing of nano- and non-nanopaint ingredients, charging the mixing vessel and agitation	Production rate: 2.5 l h^{-1} Ventilation: mobile capture hood and general ventilation Containment: no containment/process conducted over a bench top PPE: RPE and DPE	ES1. Weighing, charging and mixing ES2. Milling
Inkjet printing	A simulation study was conducted to measure the levels of release of ENPs during the preparation of silver-based inks for inkjet applications	Production rate: <1 l h^{-1} Ventilation: natural ventilation Containment: process conducted over a bench top PPE: RPE and DPE	ES1.Charging and purging ES2. Printing ES3. Cleaning

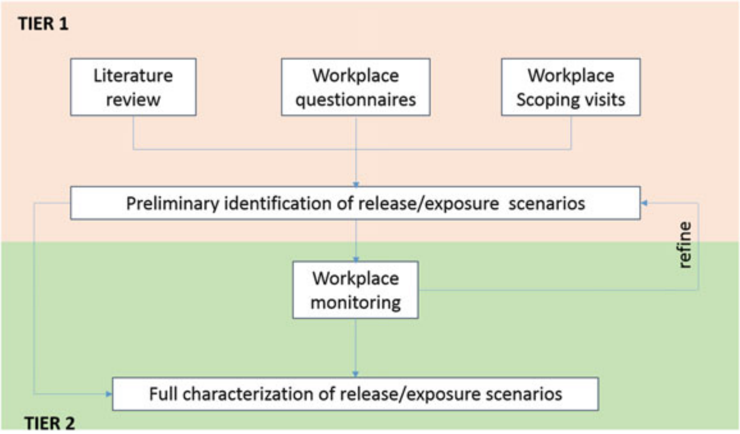

Fig. 1 Tier approach used

as well as a first scoping visit to gather information on the level of background and variations on the particle number concentration during relevant operations. The tier 2 assessment comprises a thorough study of the type and levels of particles released during selected tasks and operations. The experimental work was complemented with the analysis of peer-reviewed publications.

The approach implemented within the project is depicted in Fig. 1. It should be noticed that tier 2 evaluations were conducted when a release of ENPs is expected on the basis of the information retrieved from the scoping visit and the personalised questionnaires developed to obtain information on the potential levels and patterns of release.

The purpose of the scoping visit was to obtain a preliminary set of data on the levels of release and exposure. The analysis of the data contributed to determining appropriate monitoring approaches to characterise the levels of the release during the second-tier studies.

These tier 1 studies were performed with the support of five companies, all of them members of the NanoMICEX consortium. A suit of instruments was used to monitor the nanoparticles released in indoor facilities, including particle counters (CPC, TSI model 3007, and the Aerasense NanoTracer, Philips Electronics); an optical particle sizer (OPS – TSI model 3330), which provides data on particle size distributions; and the DustTrak (DT II – TSI Model 8532), which provides measures in terms of mass per volume (in units of mg/m^3 for 5 dust size fractions).

Tier 2 assessments consisted in a more detailed analysis of the properties of the particles released. The instrument suite defined previously was complemented with an aerodynamic particle sizer (APS) for assessing microscale particle number concentrations and size distributions and a fast mobility particle sizer (FMPS) for assessing particle number concentrations and size distributions in the nanoscale range. These second-tier measurements involved monitoring particle concentration and size distributions prior to (background) and during ENPs' manufacture and use at specific work area locations.

Several filter-based air samples (37-mm open-faced cassettes) were collected during the measures conducted in order to characterise the size, shape and composition of the ENPs released. These air samples were collected as close as possible to the suspected emission source to increase the probability of detecting any release (near field). In addition, far-field air samples were also collected. This practice is highly recommended when the levels of background NMs are significatively high.

The filters collected were further analysed by scanning electron microscopy (SEM) and/or energy-dispersive X-ray spectroscopy (EDXS) to obtain relevant morphological and compositional data.

Within NanoMICEX, the analyses of real-time measured concentrations, through comparison with background and times of workroom activities, together with the use of compositional data to inform speciation, have been used to identify and assign potential point or diffuse sources of ENPs.

Background levels of particles in the nanometre range were measured before the synthesis or processing of the ENPs to identify any increase in the levels of ENPs. It was assumed that the background levels do not fluctuate during the synthesis or processing operations.

The sources of incidental nanoparticles were also identified prior to the measurement, being broadly classified as:

1. Inside workroom (laboratory or plant room) where the ENP was being produced or used.

2. Elsewhere in the factory, i.e. outside workroom but within the factory premises (inside or immediately outside the factory buildings). This leads to considerable uncertainty in attributing the measured concentrations to ENM for dry synthesis and formulation.
3. Outside the factory, as anthropogenic and natural.

Time intervals for obtaining a size-resolved average (real-time) concentration plot may be either short, minutes in case of an activity of short duration or that of a spike or peak observed in the particle number concentration time series plot, or long-lasting hours for the duration of a long task or background sampling. The source of release can then be identified by the time log of the activities, matching the exact time at which the concentration level was measured with the time when a particular activity took place or a source was emitting.

4.4 Main Results and Conclusions

4.4.1 Synthesis of Nano-ZnO by Flame Spray Pyrolysis

The data retrieved from scoping visits showed little evidence of release of ENP during several operations conducted during the wet synthesis of ENPs. In the case of dry synthesis of TiO_2 nanopigments by flame pyrolysis (TiO_2 $d_{50} = 80$ nm), elevated particle concentrations were observed during the pyrolysis at around 90 and 250 nm compared to background.

The processes evaluated during the dry synthesis of TiO_2 included harvesting of the ENP powder, and finally the furnace shut down. Harvesting occurred intermittently during the pyrolysis reaction and at the end, and the production process is largely automated with a few manual interventions at the start and end. The reactor unit is cleaned after each production runs with solvents or clean water, depending on whether the material is changed or not.

Figure 2 shows the graphical representation of the levels of background aerosols measured in the pilot plant where the rector unit is located. Background sampling with the FMPS and APS was carried out for about 1.5 h, showing negligible levels of particles in the workroom above 523 nm, although concentrations up to 120,000 particles/cm^3 were measured at around 25 and 93 nm in the FMPS samples.

The pyrolysis measurements were taken for the last 80% of the pyrolysis stage and for furnace shutdown. During synthesis of nano-TiO_2, elevated particle concentrations were observed during the pyrolysis at around 90 and 250 nm compared to background (Fig. 3). It is possible that the initial increase is due to combustion of fuel in the furnace and possibly emissions from the hot metallic material of the pyrolysis unit itself rather than the release of any ENPs. However, there was ENP leakage from the collection vessel into the workplace atmosphere at the harvesting end of the pyrolysis unit in the latter stage of pyrolysis. This might explain the emergence of the third mode.

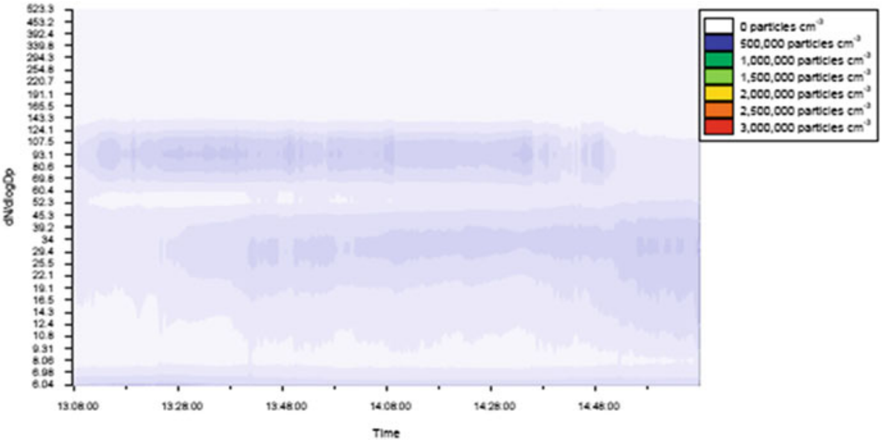

Fig. 2 FMPS background measurement

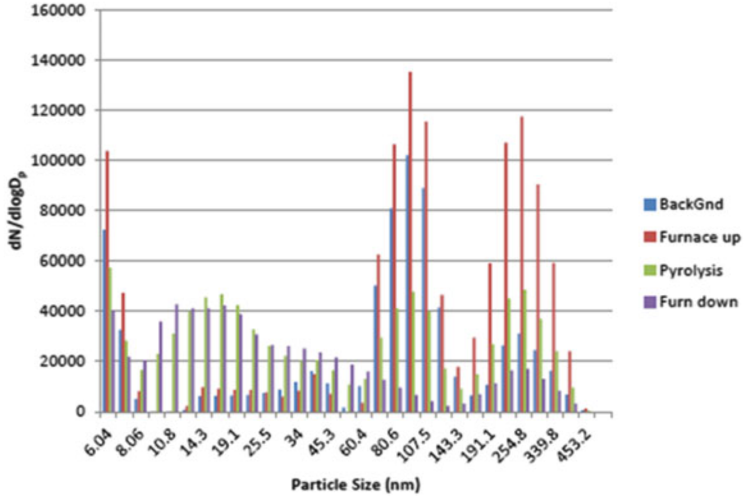

Fig. 3 Particle size distribution during the synthesis of TiO_2

The filter samples collected show in (Fig. 4) that at least some of the airborne particles contained Al, Co and Ti, all of the elements present in the molecular formula of the ENPs synthetised in the pilot plant. This may suggest that ENPs are released during the synthesis, but as Cr, Cu, Sb and Zn were also detected, it confirms that there is another source of these particles. This could be emissions from hot metal-related processes (perhaps the actual metal the pyrolysis unit is constructed from), from resuspended particles from settled dust on plant room surfaces or from activities in the warehouse area in which the plant room is located or beyond.

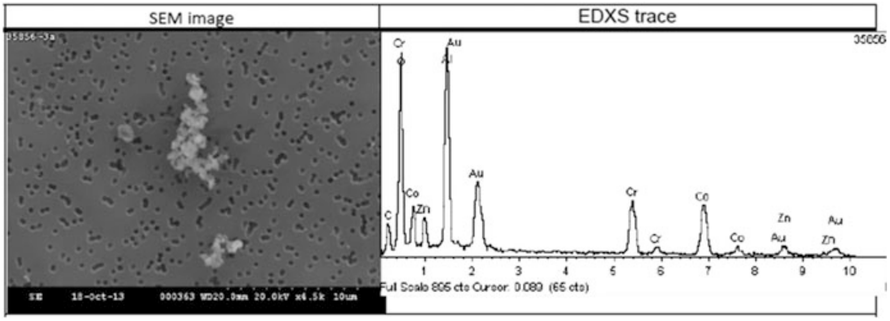

Fig. 4 High-magnified SEM image (*left*) of an airborne particle (8 μm) obtained in the far field of the harvesting zone at the pyrolysis and EDXS spectrum (*right*)

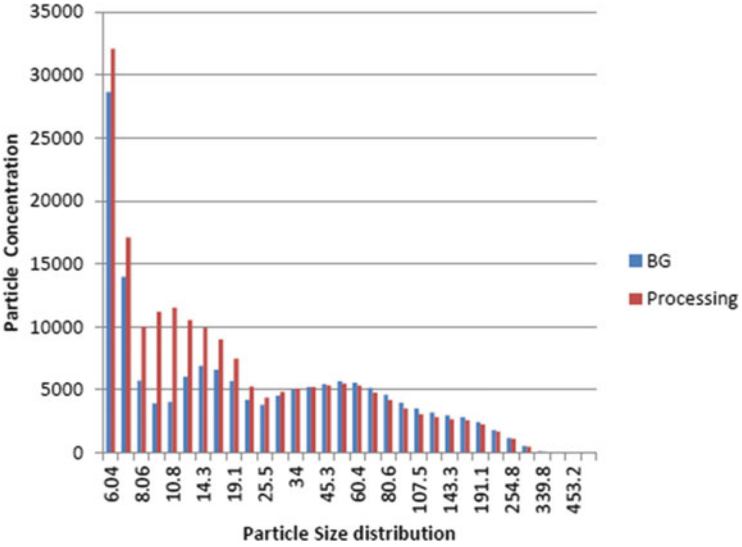

Fig. 5 FMPS showing PSD ZnO (*down*)

4.4.2 Functionalisation of Nano-ZnO

The functionalisation of ZnO (particle diameter, 98 nm) was surveyed in SME dedicated to the distribution of ENPs for several industrial sectors. Preliminary discussions with the company and measurements of a production run during the scoping visit demonstrated that wet operations were not likely to release ENPs. However, other tasks as manual vacuum drying, packaging or maintenance of the ventilation system could lead to some release of ENPs.

Background measurements with the FMPS and APS show extremely low levels of particle concentration (below 5,000 part/cm^3) in the work room. Figure 5 shows the particle size distribution in the laboratory preparation room. A trimodal PSD appeared during the preparation of ZnO NPs, with peaks at approximately 10, 45 and 160 nm.

Given that the processes are largely enclosed (glove box, fume hood and sonicator cabinet) and ventilated when using powders (glove box and fume hood), it is difficult to see how the ENPs could be released into the workplace environment during dispersion.

Samples taken inside the fume cupboard showed ZnO agglomerates present where they were being used as a raw material in the nanofluid manufacture, suggesting that levels measured by the FMPS are due to ambient dust from outside the laboratory, probably originating from the welding school area outside the laboratory and the building. On the other hand, the increases in concentration are likely to be due to the emissions from the motor driving the sonicator shaft during homogenisation.

4.4.3 Inkjet Printing Simulation

An SME dedicated to the formulation of inks was surveyed to evaluate the likelihood of release during an inkjet printing process involving the use of nano-Ag ink. The scoping visit plus information of the company showed that the main scenario of particle release was the maintenance of the fume cupboard extraction system.

None of the printing tasks are likely to generate significant release as the inks are used in solution form with a high level of containment (released dropwise from the cartridge/reservoir in an enclosed printer). Measurements carried out over a printing simulation were taken by holding the instruments close to the printer nozzle. Although there was no general ventilation in the room, the two access doors were left opened throughout the printing process, showing a decrease of concentration. Figure 6 shows the evolution of the particle number concentration at different stages of the process.

The filter samples collected are depicted in Fig. 7. The filters show some large inorganic particles and small, loosely bound organic agglomerates present. These last have a morphology consistent with agglomerates known to be originated from airborne fume, soot and possibly during the formation/formulation of nanoparticles.

Silver was not detected in either sample; thus, it seems that the elements detected were present in resuspended residual particles from previous printing runs or originate from other sources, such as during nano-Ag inkjet printing when the coating or shell is released from the surface (the Au detected is from the sample coating).

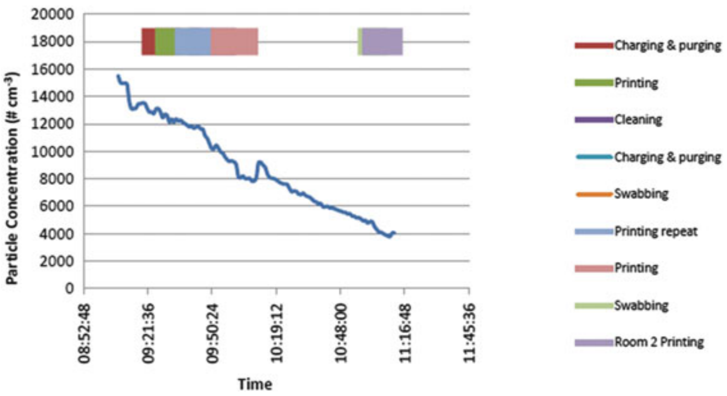

Fig. 6 CPC concentrations by task during printing process with Ag NPs

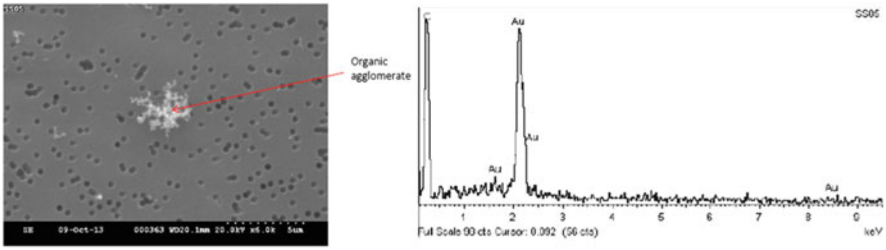

Fig. 7 SEM image (*left*) and EDXS profile (*right*) of organic particle agglomerate from sampling of laboratory atmosphere

4.4.4 Preparation of a Nano-Enabled Prototype Paint from Pristine Nanopowders

The last company surveyed was dedicated exclusively to the painting industry. In this company, the most likely scenarios for release or exposure are the places where the charging of the paint mixture with powdered ENP takes place, since there is no containment or extract ventilation.

As it is shown on Fig. 8, measurements showed that particle concentrations at 250 nm increased compared to background when the overhead stirrer blended the paint ingredients together during homogenisation. Enhanced concentrations came likely from emissions associated with the motor driving the shaft tube assembly, although several other peak concentrations were observed around 30 nm. This is considered to arise from the construction activities from an elevated platform taking

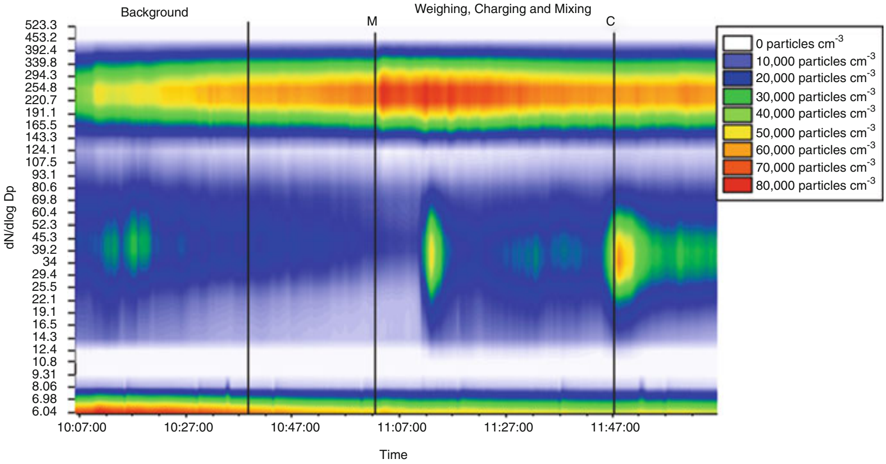

Fig. 8 PSD from FMPS measurements for ZnO and TiO_2. "M" stands for blending paint ingredients with ventilated overhead mixer while "C" for the construction works in the neighbourhood

place outside the building at laboratory window level. However, the SEM results strongly suggest that some contribution to the elevated levels could be associated also with the $CaCO_3$ additions to the paint formulation.

5 Nanoparticle Release Categories Based on Workplace Measurements

This section defines a list of release categories based on information compiled from peer-reviewed publications and data retrieved from measurement campaigns conducted by ITENE. A list of 12 nanoparticle release categories related with relevant activities and processes at all stages of the life cycle of ENP and nanoproducts has been defined.

Table 5 contains a short description of these NP release categories and related activities. These NP release categories reflect the combination of operations that may lead to a release of ENPs to the workplace environment.

Table 5 Task-specific nanoparticle release categories (NRC)

NRC	Activity	Description	Release potential	Stage
NRC1a	Synthesis process liquid-phase reaction and flame spraying	Manufacture of ENPs by process liquid-phase reaction and flame spray pyrolysis	Low	ENPs' production
NRC1b	Top-down (milling) synthesis	Manufacture of ENPs by top-down approaches	Medium	ENPs' production
NRC2a	Weighing of powders at laboratory scale (fume hood)	Weighing of small amounts of ENPs in powder forms in fume hoods		Formulation
NRC2b	Weighing of powders in open benches	Weighing of ENPs in powder forms in open benches	Medium	Formulation
NRC3a	Mixing or blending of powders for formulation of mixtures at laboratory scale (fume hood)	Mixing and blending of small amounts of ENPs into (chemical) mixtures in all types of formulating industries, such as paints, pigment paste, fuels and household products	Low	Formulation
NRC3b	Mixing or blending of powders for formulation of mixtures at laboratory scale in open benches	Mixing and blending of ENPs into (chemical) mixtures in all types of formulating industries, such as paints, pigment paste, fuels and household products	Medium	Formulation
NRC4a	Transfer of pristine NP or mixtures into small containers at non-dedicated facilities	Filling and transfer of pristine NPs and mixtures in non-dedicated facilities	Medium to high	Production/ formulation
NRC4b	Transfer of pristine NP or mixtures into small containers at dedicated facilities	Filling and transfer of pristine NPs and mixtures in dedicated facilities	Medium	Production/ formulation
NRC5a	Manual packaging (bagging) of small containers	Packaging of ENPs into small plastic containers and plastic bags (e.g. zip-closed plastic bag)	Low	Production/ formulation
NRC5b	Semiautomated packaging (bagging) of containers and bags	Packaging of ENPs into plastic containers and plastic/paper bags	Medium to high	Production/ formulation
NRC6	Formulation of ENPs in materials/polymer preparations and compounds	Mixing or blending of ENPs which will be physically or chemically bound into or onto a matrix (material) such as plastic additives in master batches or plastic compounds	Medium to high	Formulation

(continued)

Table 5 (continued)

NRC	Activity	Description	Release potential	Stage
NRC7a	Spraying operations (indoor)	Spraying of liquid formulations (e.g. paints, cleaners, lubricants and adhesives)/ indoor processing	High	Industrial use
NRC7b	Spraying operations (outdoor)	Spraying of liquid formulations (e.g. paints, cleaners, lubricants and adhesives/ outdoor processing	Very high	Industrial use
NRC8	Dyeing and finishing of textiles	Immersion operations such as dipping and pouring. ENPs are applied to a surface by dipping the article into a bath	Low	Industrial use
NRC9	Mechanical cutting, grinding, drilling or sanding of articles	Substantial thermal or kinetic energy applied to a nanoproduct by grinding, mechanical cutting, drilling or sanding	High	Industrial use

6 Discussion and Conclusion

The incorporation of ENPs into products can improve performance, efficiency and durability in various fields ranging from construction, energy management, catalysis, microelectronics, plastics, coatings and paints to consumer articles such as foods and cosmetics. However, the potential hazards resulting from human exposure during production, use or disposal have raised concerns and targeted research early on.

The release of ENPs from a determined source is a prerequisite of downstream exposure in the workplace, and therefore a better understanding of the release rates of ENPs along their life cycle is essential to evaluate the likelihood of exposure. However, despite the importance of the release on the exposure in occupational environments, little has been done so far to approach this area systematically.

New studies are starting to appear on the literature in relation with the release rates of ENPs under different operative conditions, transport mechanisms affecting the transference of released ENPs from source to receptors and effectiveness of risk management measures to reduce release. However, the current knowledge on the release of ENPs is scarce partly due to the lack of techniques suitable for collecting, preserving and storing samples containing ENPs, as well as to a poor understanding of nanomaterial properties and behaviour in the indoor workplaces. So far, scientists have not been able to fill these gaps due to a number of reasons including the fact that ENPs consist of several highly diverse class of substances, which restricts the establishment of clear release patters, as well as the lack of adequate measurement techniques and standardised testing procedures to obtain quantitative information of possible release rates of ENPs.

This chapter clearly shows a potential release of nanoparticles at all stages of the life cycle, from production, downstream use, accidental spills and consumer use to end-of-life treatments. However, there is little evidence supporting the release of the specific types of ENPs being manufactured and/or handled at industrial sites, which highlights the importance of the background aerosols and the need of clearly identifying the origin of the particles monitored and/or sampled in workplace environments, where a mixture of background aerosols (BA), process-generated nanoparticles (PGNP) and engineered nanoparticles is expected.

The data retrieved from recent studies that focused on the quantification of the release of ENPs in occupational settings show a significant release rate in processes involving the application of frictional forces and pressure, both resulting in the release of ENPs in quantities up to 2.0E10 particles/cm^3. Major concerns are expected from wide dispersive applications such as the spraying of liquid dispersions containing ENPs and grinding processes. In these processes, where the likelihood of release has been considered very likely, highly recommended is the implementation of controls to avoid the transport of the particles released from the source to the receptors.

Other conventional processes such as harvesting and cleaning operations can generate a significant release of ENPs, being highly recommend to implement administrative procedures and controls aimed at reducing the release of ENPs to background levels.

The results from the studies conducted within the FP7 project NanoMICEX demonstrated the presence of airborne nanoparticles in the workplace. However, the results from the measurement campaigns conducted within the project showed that there was little evidence of release of the target ENPs during the various activities evaluated. Qualitative (elemental) analyses of filter samples for particle composition, together with a (time) log of when release-related activities occurred, were used to try and assign airborne concentration measurements to nanoparticle release sources and activities in the workroom.

Gaps in activity data, the inability to relate company ENP size data to measured dN/dlogDp for an emission, the impossibility of monitoring at all potential sources simultaneously and the assumption that the initial background reading does not fluctuate lead to difficulties in assigning measurements to ENP release.

Moreover, the considerable opportunity for contributions to the release of incidental NP from inside the workroom (where the ENP was being produced or used), elsewhere in the factory (on the company premises) and outside the factory (off the company premises) leads to considerable uncertainty in attributing the measured concentrations to ENP for ENP synthesis processes and production (formulation).

In general terms, the data retrieved from the measurements showed that particle concentrations at 250 nm increased compared to background and that there were some episodes of elevated particle number concentrations below 100 nm, although it was not clear whether this was associated with handling of nanopowders and/or mixing operations.

The data compiled from the peer-reviewed publications were analysed to cluster relevant activities according to the likelihood of release. It is commonly accepted that wide dispersive uses such as spraying can lead to a significant increase in the amount of ENPs released in the workplace. A list of release categories has been proposed to support the evaluation of the potential release in common operations.

It shall be noticed that there is a current lack of data on the release rate of nanoparticles from conventional sources, which limits the development of accurate predictive models commonly used for risk assessment purposes. Similarly, the mechanism affecting the transport of the ENPs released is not sufficiently understood; therefore, the nature and extent of the exposure to nanoparticles in workplaces can only be defined measuring and characterising the size and chemical nature of the ENPs detected in the breathing zone (PBZ) of workers exposed to ENPs.

The outcomes of the studies conducted to develop this chapter show that, in practice, each situation should be treated differently in terms of release considerations. A thorough analysis of the possible sources of release and modifying factors should be completed prior to adequately conducting quantitative assessment of the levels of exposure in workplaces. This assumption does not imply the lack of a specific pattern in the release behaviour of ENPs.

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References

1. Savolainen K et al (2013) Nanosafety in Europe 2015–2025, Finnish Institute of Occupational Health/EU NanoSafety Cluster
2. Kumar A et al (2013) Manual on critical issues in nanotechnology R&D management: an Asia-Pacific perspective. APCTT-ESCAP. http://nanotech.apctt.org/Nanotech%20Manual%20-%20Chapter%201.pdf
3. Roco MC et al (2011) Nanotechnology research directions for societal needs in 2020: retrospective and outlook. NSF/WTEC report, Springer. http://www.wtec.org/nano2/Nanotechnology_Research_
4. Yokel RA (2011) Engineered nanomaterials: exposures, hazards, and risk prevention. J Occup Med Toxicol 6:7
5. Brouwer D (2010) Exposure to manufactured nanoparticles in different workplaces. Toxicology 269:120–127
6. Karjalainen A et al (2012) Background information on exposure, use, and hazard of manufactured nanomaterials in the construction sector. Scaffold Deliverable 1.2. http://scaffold.eu-vri.eu/filehandler.ashx?file=13722

7. Wu Q et al (2010) Behaviour of aerosol particles released into simulated workplace environment. NSTI-Nanotech 3. http://cordis.europa.eu/documents/documentlibrary/124584951EN6.pdf
8. Schneider T et al (2011) Conceptual model for assessment of inhalation exposure to manufactured nanoparticles. J Expo Sci Environ Epidemiol 21(5):460–463
9. Fransman W et al (2009) Development of a mechanistic model for the advanced REACH Tool (ART). TNO Report V8667, The Netherlands
10. Jianjun N et al (2015) Spatial and temporal variability of incidental nanoparticles in indoor workplaces: impact on the characterization of point source exposures. Environ Sci Process Impacts 17:98–109
11. Methner M et al (2009) Nanoparticle emission assessment technique (NEAT) for the identification and measurement of potential inhalation exposure to engineered nanomaterials. J Occup Environ Hyg 7(3):127–132
12. Asbach C et al (2012) NanoGEM: Standard Operation Procedures for assessing exposure to nanomaterials, following a tiered approach. Tiered Approach for the assessment of exposure to airborne nanoobjects in workplaces
13. Witschger O et al (2012) Recommendations for characterizing potential emissions and exposure to aerosols released from nanomaterials in workplace operations. Hyg Secur Trav 226:41–55
14. van Broekhuizen P et al (2012) Exposure limits for nanoparticles: report of an international workshop on nano reference values. Ann Occup Hyg 56(5):515–524
15. Filipponi L (2007) Nanotechnoly: a brief introduction. nanoparticles in the atmosphere. FP6 NanoCAP
16. Wehner B et al (2002) Particle number size distributions in a street canyon and their transformation into the urban-air background: measurements and a simple model study. Atmos Environ 36:2215–2223
17. Donaldson K et al (2005) Combustion-derived nanoparticles: a review of their toxicology following inhalation exposure. Part Fibre Toxicol 2:10
18. Szymczak W et al (2007) Emission of ultrafine copper particles by universal motors controlled by phase angle modulation. Aerosol Sci 38:520–531
19. Van Broekhuizen P et al (2012) Exposure limit values for nanomaterials. capacity and willingness of users to apply a precautionary approach. J Occup Environ Hyg 10:46–53
20. Bémer D et al (2010) Ultrafine particles emitted by flame and electric arc guns for thermal spraying of metals. Ann Occup Hyg 54:607–614
21. Elihn K (2009) Ultrafine particle characteristics in seven industrial plants. Ann Occup Hyg 53:475–484
22. Pfefferkorn F et al (2010) Characterization of exposures to airborne nanoscale particles during friction stir welding of aluminum. Ann Occup Hyg 54:486–503
23. Beurskens-Comuth PA et al (2011) Video exposure monitoring as part of a strategy to assess exposure to nanoparticles. Ann Occup Hyg 55(8):937–945
24. Topham N et al (2012) Control of Cr6+ emissions from gas metal arc welding using a silica precursor as a shielding gas additive. Ann Occup Hyg 56:233–241
25. Ramachandran G et al (2011) A strategy for assessing workplace exposures to nanomaterials. J Occup Environ Hyg 8(11):673–685
26. Seipenbusch M, Yu M, Asbach C, Rating U, Kuhlbusch T, Lidén G (2014) From source to dose: emission, transport, aerosol dynamics and dose assessment for workplace aerosol exposure. In Handbook of nanosafety: measurement, exposure and toxicology, pp 135–171
27. Stanley NJ (2010) The fate of airborne nanoparticles released from a leak in a nanoparticle production process into a simulated workplace environment. Ph.D. dissertation, University of Minnesota. https://conservancy.umn.edu/handle/11299/98009
28. Boowook K et al (2014) Assessment of nanoparticle exposure in nanosilica handling process. Ind Health 52:152–162
29. Kuhlbusch TAJ et al (2011) Nanoparticle exposure at nanotechnology workplaces: a review. Part Fibre Toxicol 8:22

30. Maynard AD et al (2004) Exposure to carbon nanotube material: aerosol release during the handling of unrefined single-walled carbon nanotube material. J Toxicol Environ Health 67:87–107
31. Evans DE et al (2013) Dustiness of fine and nanoscale powders. Ann Occup Hyg 57 (2):261–277
32. Tsai S et al (2008) Airborne nanoparticle release associated with the compounding of nanocomposites using nanoalumina as fillers. Aerosol Air Qual Res 8(2):160–177
33. Hämeri K et al (2002) The particle detection efficiency of the TSI-3007 condensation particle counter. Aerosol Sci 33:1463–1469
34. Frogget SJ (2014) A review and perspective of existing research on the release of nanomaterials from solid nanocomposites. Part Fibre Toxicol 11:17
35. Park J et al (2009) Characterization of exposure to silver nanoparticles in a manufacturing facility. J Nanopart Res 11:1705–1712
36. Leppänen M et al (2012) Exposure to CeO(2) nanoparticles during flame spray process. Nanotoxicology 6(6):643–651
37. Walser T et al (2012) Exposure to engineered nanoparticles: model and measurements for accident situations in laboratories. Sci Total Environ 420:119–126
38. Koponen IK et al (2013) Study on nanoparticle aerosol emission and evolution using laboratory scale liquid flame spray nanoparticle generation system. FP7 Nanodevice Deliverable 5.2. http://www.researchgate.net/profile/Cindy_Bekker/publication/269702810_Field_and_Laboratory_Measurements_Related_Occupational_and_Consumer_Exposures/links/54a11b590cf257a63602248a.pdf; http://www.nano-device.eu/fileadmin/user_upload/_temp_/pictures/NANODEVICE/publications/Schneider_etal_2011_JESEE.pdf
39. Ogura I et al (2011) Release potential of single-wall carbon nanotubes produced by super-growth method during manufacturing and handling. J Nanopart Res 13:1265–1280
40. Sally S et al (2015) Quantitative exposure and contextual data for key exposure scenarios. Deliverable 4.2. NanoMICEX project
41. Kaminski H et al (2015) Measurements of nanoscale TiO_2 and Al_2O_3 in industrial workplace environments – methodology and results. Aerosol Air Qual Res 15:129–141
42. Brouwer D et al (2009) From workplace air measurement results toward estimates of exposure? Development of a strategy to assess exposure to manufactured nano-objects. J Nanopart Res 11(8):1867–1881
43. Koivisto AJ et al (2012) Industrial worker exposure to airborne particles during the packing of pigment and nanoscale titanium dioxide. Inhal Toxicol 24(12):839–849
44. Dylla H et al (2012) Characterization of nanoparticles released during construction of photocatalytic pavements using engineered nanoparticles. J Nanopart Res 14(4):825
45. Norgaard AW et al (2009) Release of VOCs and particles during use of nanofilm spray products. Environ Sci Technol 43:7824–7830
46. Chen BT et al (2010) Nanoparticles-containing spray can aerosol: characterization, exposure assessment, and generator design. Inhal Toxicol 22:1072–1082
47. Schlagenhauf L et al (2012) Release of carbon nanotubes from an epoxy-based nanocomposite during an abrasion process. Environ Sci Technol 46(13):7366–7372
48. Van Landuyt KL et al (2014) Nanoparticle release from dental composites. Acta Biomaterialia 10:365–374
49. Fleury D et al (2011) Identification of the main exposure scenarios in the production of CNT-polymer nanocomposites by melt-moulding process. J Cleaner Prod 53:1–15
50. Faghihi EM et al (2015) Are there generalizable trends in the release of airborne synthetic clay nanoparticles from a jet milling process? Aerosol Air Qual Res 15:365–375
51. Tielemans E et al (2008) Conceptual model for assessment of inhalation exposure: defining modifying factors. Ann Occup Hyg 52(7):577–586
52. Cherrie JW et al (2011) Revisiting the effect of room size and general ventilation on the relationship between near- and far-field air concentrations. Ann Occup Hyg 55(9):1006–1015

53. Tieldmans E et al (2008) Conceptual model for assessment of inhalation exposure: defining modifying factors. Ann Occup Hyg 52(7):577–586
54. van der Schaaf D et al (2006) The “Substance Manager”, a generic tool for SMEs to control chemical risks at work. Part 1: background, capabilities and future developments. Book of abstracts, BOHS conference 2006. http://www.nature.com/jes/journal/v17/n1s/full/7500604a.html
55. Tsai SJC et al (2009) Airborne nanoparticle exposures associated with the manual handling of nanoalumina and nanosilver in fume hoods. J Nanopart Res 11:147–161
56. Yeganeh B et al (2008) Characterization of airborne particles during production of carbonaceous nanomaterials. Environ Sci Technol 42:4600–4606
57. Johnson DR et al (2010) Potential for occupational exposure to engineered carbon-based nanomaterials in environmental laboratory studies. Environ Health Perspect 118(1):49–54
58. Bello D et al (2010) Exposures to nanoscale particles and fibers during handling, processing and machining of nanocomposites and nano engineered composites reinforced with aligned carbon nanotubes. In: ICCM-17 proceedings, Edinburgh, Scotland July 27–31, 2009. http://iccm-central.org/Proceedings/ICCM17proceedings/Themes/Nanocomposites/PROCESS%20OF%20NANOCOMP/E7%2013%20Bello.pdf
59. Cena LG, Peters TM (2011) Characterization and control of airborne particles emitted during production of epoxy/carbon nanotube nanocomposites. J Occup Environ Hyg 8:86–92
60. Tsai SJ et al (2008) Airborne nanoparticle release associated with the compounding of nanocomposites using nanoalumina as fillers. Aerosol Air Qual Res 8:160–177
61. Köhler A, Som C, Helland A, Gottschalk F (2008) Studying the potential release of carbon nanotubes throughout the application life cycle. J Clean Prod 16(8–9):927–937
62. Vance ME et al (2014) Exposure to airborne engineered nanoparticles in the indoor environment. Atmos Environ 106:503–509

Nanomaterials Release from Nano-Enabled Products

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Abstract Nanomaterials release quantification and characterization is crucial for risk assessment studies, and experimental simulation studies provide the most concrete basis for estimating the release of nanomaterials in any stage of its life cycle. Nanomaterials are used in a broad range of applications, in different forms (embedded, as coatings, suspended, etc.) and with different size ranges. With all these variables, the number of scenarios where release of nanomaterials could occur is huge. In this chapter, we aim to review use-phase release scenarios that are usually considered in the literature, as well as the results of such studies and the protocols used for product ageing and for nanomaterial quantification and characterization. Finally, we point out the gaps in nanomaterials release studies and identify future research needs.

Keywords End user, Exposure, Nano-enabled products, Nanomaterials, Release, Risk

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1 Introduction

Much research in recent years has primarily focused on nanomaterial (NM) hazard and potential exposure in the workplace, which have raised awareness to occupational safety needs in machining processes such as sanding or cutting [1]. These activities are commonly performed indoors or in enclosed environments. Thus, when potential risk is determined, exposure to NMs can be minimized by applying appropriated mitigation plans. However, during the common use of products containing NMs, namely nano-enabled products, these can spread and be exposed to much uncontrollable conditions, increasing the potential impact on humans and the environment. Over the past decade, NM use and diversity of applications have grown extensively and continue to grow rapidly [2]. Therefore, NM release from commercial products must be identified and studied to adequately prevent and treat any eventual release to the environment, if those NMs suppose a risk.

1.1 Global Market of Nanomaterials and Evolution

As key enablers for a whole new generation of products, NMs reached the market long ago in multiple sectors. These nano-enabled products are present on the markets of polymers, batteries, 3D printing compounds, displays and filtration membranes or coatings, among others, and in 2014 gained presence in especially relevant sectors such as the medical industry, energies, new technologies (e.g., nanowires) or surface treatments. Table 1 summarizes the most common properties that NMs provide to the different sectors.

Multiple reports have been published to date analysing the market. However, reliability of those analyses is unclear, since registration of nano-enabled products is not compulsory (except in France and Denmark) and is mainly based on data obtained from companies by direct inquires. Two databases (Woodrow Wilson and RIVM, the Dutch National Institute for Public Health and the Environment)

Table 1 Representative properties associated with the current nanotechnology applications on different sectors

Property	NMs most common used	Mechanism of action	NM spatial distribution
Antibacterial	Ag, TiO_2, SiO_2	Release of active species (e.g., Ag^+), photocatalytic degradation, dry conditions	Surface, embedded
Self-cleaning, stain resistance	TiO_2, SiO_2, CNT, nanofibres	Tailored wettability by contact angle modification, photocatalysis	Surface
Mechanical	CNT, nanofibres clays, SiO_2, TiO_2	Improved stiffness, damage and wear resistance, strength due to matrix reinforcement	Embedded
Magnetic	Fe, Fe_xO_y	Inclusion of magnetic materials	Embedded, dispersions
Controlled release	Organic capsules, Au	Release of active ingredients, activated by external stimuli or matrix degradation	Surface, dispersions
Fire retardant	Clays, polymer nanocoatings, CNT, SiO_2	Insulation	Surface, embedded
UV blocking	ZnO, TiO_2, SiO_2	UV light absorption	Surface
Electrically conductive, luminescent	Cu, CNT, carbon black, quantum dots, Ag, Au	Addition of conductive and photo- and electroluminescent properties	Embedded, surface
Filtration/adsorption capacity	Nanofibres with or without adsorbed NMs (e.g., Fe_3O_4)	Retention governed by pore size and nature of the NM	Surface
Barrier	TiN, clays, SiO_2	Air, water, CO_2 blocking in packing materials	Embedded
Pigments	TiO_2, carbon black, Fe_xO_y, $BaSO_4$	Wavelength-selective absorption	Surface, embedded

revealed that in 2014, silver, titanium and carbon-based NMs were the major NMs associated with consumer products [3]. Though uncertainty exists, the market of (micro/nano)electronic components seems to be the most expanded, representing around $215 billion of value globally [4].

Nanocoatings are gaining market share and have one of the biggest potentials in industry. According to a recently published global report, the antimicrobial treatments ranked as the highest consumed type of nanocoatings, accounting for 30% of the worldwide demand in 2012 [5]. Indeed, sectors such as the medical, healthcare, food manufacturing and water treatment industry extensively depend on the use of antimicrobial nanocoatings. As an example, only the catheter market constituted more than $22 billion globally in 2012 [6], and growth of drug-resistant bacteria (which cause infections in 10% of catheterized patients) can be prevented using silver or TiO_2 nanocoatings.

It is very difficult to quantify, or even estimate, the levels of nanocomposite (NC) production and the amounts of every NM that are being used due to the lack of official registers and the mistrust of the companies in giving any type of information

[7–9]. Anyway, all the attempts to estimate annual production of NMs point to NCs as one of the most important application fields, mainly as plastic reinforcers (which include the packing industry). Sun et al. claimed that NMs use in polymer reinforcement represented the main production of carbon nanotubes (CNT, 84.1%, >300 tons/year in EU) and fullerenes (45.9%) and an important application field of other nanosized materials such as TiO_2 (3.6%, >500 tons/year in EU), ZnO (2%, >1,000 tons/year in EU) or Ag (3.3%) [9]. Similarly, Kalinina has reported plastic reinforcement as one of the main uses of nano-SiO_2, estimating around 1,500 tons/year in EU [8, 10]. These studies also report the penetration of NMs in ceramic and metallic materials.

Likewise, there is a huge potential in developing safe nanoparticle-based products for medical use apart from coatings, and continued growth is expected in emerging economies such as China, Russia or Brazil. According to the ETP Nanomedicine, over 200 nanotherapeutic products existed worldwide in 2014, of which 122 were nanomedical products in clinical trials [11]. The nanoparticle (NP) drug/delivery market presents an increasingly significant part of the overall pharmaceutical product market worldwide, and in 2016, the global nanomedicine market is expected to grow to almost $100 billion, one half of which is due to anticancer products [11, 12].

In the cosmetics sector, NMs have been used for decades, and their nature and application are really extensive, such as organic nanocapsules containing anti-ageing active ingredients or TiO_2 NPs used in sunscreens. Cosmoceutical formulations reached a global market of around $17 billion in 2014 [13] and are estimated by recent reports to reach $32 billion by 2016, with a high potential in Asia [14]. Finally, in food industry, NMs are used as direct food additives as well as in the packaging [15].

1.2 Regulation and Guidelines to Evaluate Nanomaterials Release

Considering the market evolution and nanosafety concerns, the necessity of specific regulations for NMs and nano-enabled products is into debate worldwide. However, due to the relative shortage of research into this topic, data available to assess exposure during nano-enabled material use is scarce and almost no specific statutes or regulations relating to NMs have been established yet. Specifically, literature supports for method validation and standardization as well as for the understanding of how the release scenarios performed at the lab scale relate to real-world conditions [16].

Regulatory requirements for NMs are most prominent in the European Union, United States and Canada, but worldwide, many other countries are developing new regulatory frameworks in risk assessment.

The European Chemicals Agency (ECHA) considers that NMs can be registered and notified as any other substance under REACH, CLP and Biocides regulations, but it clearly indicates that NMs are independent substances and cannot be notified as their bulk form. Besides, ECHA is introducing amendments/annexes in the guidelines for NM evaluation, mostly based on RIP-oN 2 and RIP-oN 3 reports [17, 18]. Similar requirements were introduced in other directives such as cosmetic [19], food [20] and medical devices [21]; however, the European Commission considers "current legislation on medicinal products allows an appropriate risk/benefit analysis and risk management of NMs" [22]. Currently in the United States, the safety assessment of NMs when used in consumer products is under discussion by the Food and Drug Administration (FDA) and the Environmental Protection Agency (EPA), and the same is being done in Canada. The FDA published in 2014 some guidances about NMs in products under its control (cosmetics, food, food contact and animal food), but they are only nonbinding recommendations. The EPA posted in April 2015 a proposed rule that is open for comments till July 2015, where they suggest to report any NM as a new chemical substance, similarly to ECHA but excluding NMs that dissolve [23]. In Europe, the use of synthetic amorphous SiO_2 as a biocide in insecticides has been recently approved [24]. This is the first biocide registered as a NM form, though it is actually composed of stable aggregates in the microscale.

The major problem at the moment is the lack of information in the quantity of NMs and nano-enabled products in the market. France (since January 2013) and Denmark (since June 2014) established the only compulsory registries for nano-enabled products [25, 26]. In order to partly compensate such limited knowledge, some collaborative initiatives exist aiming to create real inventories for the exchange of accurate information of nano-enabled consumer products that are entering the marketplace, such as the (US) Nanotechnology Consumer Products Inventory [15]. However, such repositories can only reflect general trends, and their accuracy is questionable.

Furthermore, most companies that incorporate any type of NM in their products do not explicitly claim it. Most of the data published to date relies solely on individual market report values, personal communications, surveys, reports or presentations, which generally lead to under- or overestimations. The creation of such repositories is especially relevant when researchers aim at determining existing levels of NMs in the environment by modelling predicted environmental concentrations [9].

1.3 Exposure Scenarios for Humans and the Environment

NM release from nano-enabled products depends to a great extent on several factors, such as the intended use, the stresses that the product will suffer or environmental factors the product will be exposed to, as well as the distribution of NMs within the nano-enabled product (Fig. 1). Based on these factors, several divisions can be established depending on (a) intended or unintended release, (b) physical stresses and chemical degradations that the nano-enabled product will suffer during their use (e.g., outdoor/indoor use, abrasion expected or not, contact with liquids or chemicals, etc.) and (c) potential transformation of NMs and the matrices that may occur during its use.

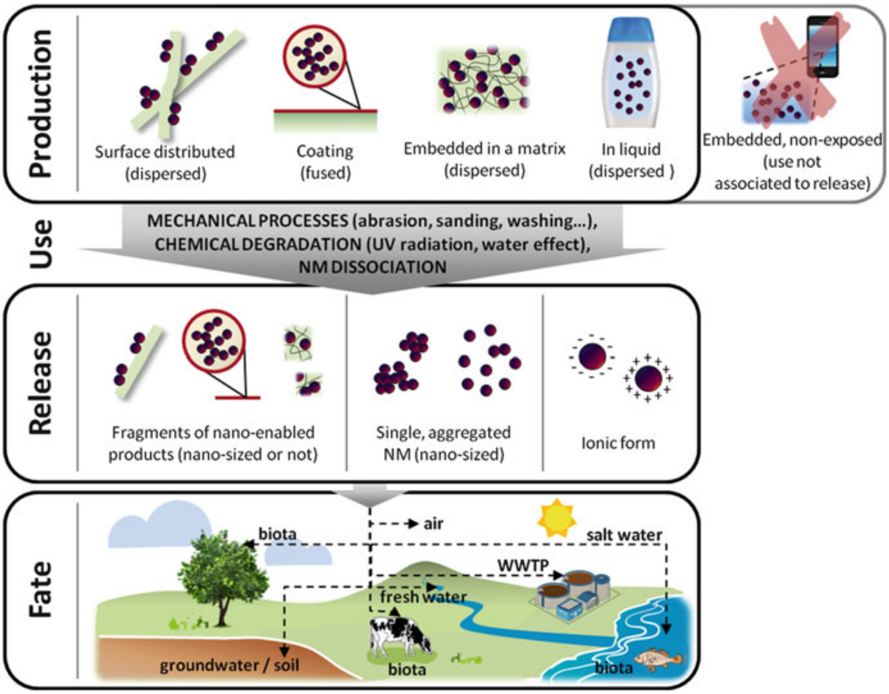

Fig. 1 Most common types of nano-enabled products considering NM distribution and possible forms of NMs released during the use of these products that can end up into the different environmental compartments

Therefore, it is crucial when trying to draw an experimental programme of data collection to identify critical exposure/release scenarios and map them across the three domains: occupational, consumer and environment. This includes in each case the definition of the action/activity that might cause the release of NMs, the transformations that the NMs investigated might suffer, and the exploration of the techniques that will allow a reliable characterization and quantification of a released NM.

Some of the existing nano-enabled products will enter the environment intentionally, such as the Fe^0 NPs for groundwater remediation or the NMs contained in agrochemicals. Similarly, the total amount of TiO_2 NMs included in cosmetic formulations and applied on human skin will enter the environment after showering, regardless of any protective measures implemented.

On the other hand, during the use of other types of nano-enabled products (e.g., paints), NMs included in solid matrices will be unintentionally released, as free NMs or attached/integrated in the matrix, due to progressive degradation (weathering or mechanical processes such as abrasion) [27]. Figure 1 and Table 2 show the most common types of nano-enabled products when considering NMs distribution and the most probable release scenarios.

Table 2 Examples of existing nano-enabled products. Possible release of NMs contained during its use and predictable exposure are also listed

Product category	Most common NMs	Release extent/ time frame	Exposure	Factors affecting release	Release forms
NCs exposed to weathering	CNT, SiO_2, TiO_2, ZnO	Low/ continuous	E (WWTP, soil)	Type of polymer and NM, compatibilization, NM concentration	Matrix particles with embedded or protruded NMs (mainly), free NMs (rare)
NCs exposed to abrasion	CNT, SiO_2, TiO_2, ZnO	Low–high/ continuous	H/E (air)	Type of polymer, energy input, environmental conditions	Matrix particles with embedded or protruded NMs (mainly), free NMs (rare)
Textiles	Ag, TiO_2	Medium–high/ continuous	H/E (WWTP)	NM concentration, adhesion strength, type of NM	Individual/ aggregated NMs with or without associated textile fragments. If dissociation occurs, other species form
Paints (outdoors)	TiO_2, SiO_2, Ag	Low/ continuous	E (WWTP)	Matrix composition, environmental conditions	NMs embedded in the organic matrix, aggregated and few dispersed single NMs (it has been shown that coating is still present on NM surfaces)
Cosmetic and personal care products	TiO_2, ZnO	High/ intermittent	H/E (seawater/ freshwater, WWTP)	n.a.	NMs embedded in the organic matrix and aggregates of free NMs

(continued)

Table 2 (continued)

Product category	Most common NMs	Release extent/ time frame	Exposure	Factors affecting release	Release forms
Food contact materials	TiN, SiO_2, carbon black	Very low/continuous	H/E	Compatibilization, matrix	Individual/ aggregated particles (dissociation might occur depending on the NM)
Food additives	SiO_2, calcium silicate	High/ intermittent	H/E (WWTP)	n.a.	Particles or dissociated ions

NCs nanocomposites, *E* environment, *H* human

In this chapter, a comprehensive overview of the state of the art concerning the release during the use phase of nano-enabled products is presented, divided by the type of product in four different sections.

2 Nanocomposites

2.1 Introduction and Applications

Nanocomposites (NCs) are multiphase solid materials that have at least one of the phases in the nanoscale. Though strictly speaking any nano-enabled solid material is a NC, the most common is to use "NC" for solid matrices that contain embedded NMs and classify materials surface-treated with NMs such as textiles and paints in specific categories.

Nowadays, one can find almost any type of NM in any type of matrix to produce a material with enhanced or new attributes, and several of these applications have reached the market, even in mass commodity products. It is well known that NC properties depend on its constituents and on the production methodology, as the distribution of the NMs in the matrix strongly affects NC performance (homo- or heterogeneous, compatibilization, aggregation/agglomeration state, etc.) [28–30].

NCs are usually divided into three different categories:

- *Polymer-matrix NCs* (also known as nanofilled polymer composites). They are the most studied and, so, developed NCs. Nano-reinforcement of polymers can dramatically enhance or even change their properties, so these hybrid materials have been used in several applications such as for mechanically strengthening, UV filtering, acceleration of bio-/photodegradability, flame retardancy/fire resistance or as antistatic barriers (see Table 1). All the important industrial sectors (i.e., automotive, packaging, military or construction) have capitalized these enhanced properties.

- *Ceramic-matrix NCs*. Ceramics are fragile materials and NM additivation is largely used for their reinforcement, conferring enhanced ductility and stress resistance. This allows obtaining improved construction materials and also new applications such as armours, surgery materials or artificial bones. Ceramics have traditionally been reinforced with metallic NPs [31], but nowadays one can find in the literature ceramics reinforced with almost any type of NM (i.e., carbon-based NMs [32, 33], nanometal oxides [34] or quantum dots [35]).
- *Metal-matrix NCs*. Despite the promising findings in recent years, metal-matrix NC materials are still in their infancy, and most of them are far from the market, probably due to their cost and the difficulties in its preparation [36, 37]. This type of NCs has a great potential in the energy and aeronautic sectors because they show a combination of ceramic and metallic properties.

2.2 Nanomaterials Release During Nanocomposites Use Phase

Due to their multiple applications, several release scenarios from NCs can be identified. However, NCs are mostly used as structural materials in long-lasting products, where no or low release during long time is expected [38]. When a NM is embedded in a matrix, its release occurs in parallel to matrix degradation or abrasion. Thus, the processes to study NM release can be very similar to the ones accepted and standardized to study material performance by traditional ageing. Most literature in the field is focused on two types of degradation processes, UV ageing/weathering and machining abrasion, while literature reporting migration due to contact with liquids is still very scarce [8, 39]. These processes intend to simulate the release that occurs in different scenarios: in outdoor applications where NCs are exposed to sunlight, temperature and/or rain exposure; in NCs contacting to any type of liquid such as the ones for packaging or engineered tissue applications; and in NCs subject to abrasion forces such as in machinery applications.

2.2.1 Nanomaterials Release Studies: UV-Ageing Simulations

Numerous publications have simulated release scenarios using existing (adapted) standardized methods in order to study its response to UV exposure alone or, in other more complex scenarios, combining UV exposure with simulated rain (e.g., artificial ageing for plastics, ISO4892-2 or ISO2812-2). Examples of polymers usually investigated are epoxy resins [40, 41], polyamide [42] and polyurethane

[43], which can contain different types of nanofillers, typically CNT, SiO_2 and TiO_2 NPs. It is well established that polymeric matrices exposed to weathering can exhibit photodegradation, consequently causing oxidation and chain scission [44]. Moreover, some polymers such as polyamide are sensitive to both UV radiation and water [45], which can also cause changes in the stiffness, interfacial strength, plasticization, etc. [46]. Chemical degradation of the NCs is normally studied by a combination of ATR-FTIR and XPS.

One of the first works was published by Nguyen and co-workers, who investigated degradation of epoxy NCs under UV light and controlled temperature and humidity, using the Simulated Photodegradation via High Energy Radiant Exposure (SPHERE), equiparable to approximately 22 times the intensity of the sun at the earth surface [47]. The authors were able to detect release of SiO_2 NPs by using a special sample collector during the exposure and with the help of SEM-EDX. In other similar works, the release of NMs could not be detected (or in some cases was directly not measured) and only surface degradation was assessed [48, 49]. Morphological changes on NCs surface can be systematically followed at the nano- and microscale by atomic force microscopy and laser scanning confocal microscopy, respectively. A conceptual model describing the release of SiO_2 from the epoxy resin under UV radiation was hypothesized by Nguyen and co-workers [50]. In the first step, the surface of the polymer exhibits photodegradation by UV exposure. As a consequence, NMs tend to accumulate on this region because of the removal of the polymeric layer. According to this approach, at some point defined as the critical SiO_2 concentration/thickness at the surface, NM release starts to occur. The main disadvantage of this model is that it does not consider other external factors, such as vibration or rain water, which can accelerate NM release and/or polymer degradation.

However, it has been demonstrated that when using CNT as fillers in a polymer, these normally remain as an entangled network once the material has been exposed to UV light [51] or even after machining [52]. This shows that CNT, in contrast to that reported for SiO_2 NPs, are not spontaneously released from degraded matrices [53]. Recent work have shown further results in this area by combining UV exposure scenarios and the application of secondary mechanical forces [53, 54]. This has been accomplished by immersing the aged specimens in sonication baths. This method allows detaching the NMs deposited on the surface of the materials, and it is easily reproduced. Moreover, sonication conditions might be adapted to different levels to evaluate the energy applied to the sample. This approach has been recently validated in an interlaboratory research work [53] and has been recognized as a good candidate to complement standard processes recommended in the literature.

As a summary, the results indicate that the release of isolated NMs is barely detected as they are rarely freed from the matrix and mainly remain embedded. It means that different NMs in the same matrix can have similar characteristics once released [8]. However, due to photodegradation, hydration and hydrolysis processes, NMs can be modified and released with surface modifications (e.g., TiO_2 surface hydration or CNT oxidation). Therefore, the quantification and characterization of released NMs becomes crucial to predict posterior fate and potential hazards.

2.2.2 Nanomaterials Release Studies: Abrasion Simulations

Most of the abrasion simulations over NCs are focused on studying potential NM releases in machining processes during nano-enabled products manufacturing. Consequently, the experimental design is not ideal for use-phase abrasion studies. But machining processes have received so much attention that almost half of the studies on NM release from NCs are focused on these processes [39].

From the different machining processes found in the literature (cutting/sawing, grinding, shredding, sanding and drilling), abrasion studies based on standard protocols would be the most useful as worst-case scenarios for NM release during the use phase [39]. These studies mainly are done with a Taber abraser [43, 51, 55–60], and most of them conclude that NMs are usually released embedded in small portions of the matrix. Only two publications report significant release of isolated NMs when the NC is abraded with a Taber [55, 60]. Finally, it is clearly shown that the matrix plays an important role in preventing the release of free NMs, while the nano-reinforcement only helps in the overall resistance of the composite.

3 Paints and Inks

3.1 Introduction and Applications

The use of nano-additives in paints, lacquers and other types of coatings is an important application area, primarily intended to protect vehicles, machinery, buildings and everyday objects. NMs are generally tailored to increase the scratch resistance and surface hardness of coatings, to improve UV light resistance, to achieve better interaction between the coating and the material, to increase corrosion protection and to provide protection against microbial, physical or chemical deterioration [61–63].

Examples of widely used NMs are $BaSO_4$ and iron oxides which have been long used as coloured pigments in the automotive sector or TiO_2 (rutile) which gives a bright white color to paints. Mixtures of Al_2O_3 and SiO_2 NPs have shown great potential as anti-slip coatings on ceramic surfaces, and different types of surfaces (e.g., tiles, bricks) with self-cleaning properties have been designed by the use of TiO_2-based photocatalytic NMs. Another potential application is to use NMs on which a biocide is adsorbed in antifouling paints, to prevent premature detachment of the biocides [64].

Little is known about the use at industrial scale of NMs in commercial inks or pigments for inkjet/laser printers or other photocopy devices. Although primary toner particles typically posses diameters above 1 μm, recent studies suggest that several types of NMs might currently be used to a great extent in the ink industry [65]. These include fumed SiO_2 for enhanced flow and charge stability, TiO_2 and Fe_3O_4. In addition, the presence of several other elements, such as Sn, Mn and Al, has been also confirmed but at much lower concentrations [66].

Likewise, NMs have shown great potential in printed electronics since inks containing metal NPs (e.g., Ag) can be used to obtain highly conductive patterns using low-cost and roll-to-roll processes (such as inkjet printing) [67]. Similarly, ink formulations consisting in emissive quantum dots (e.g., CdSe, CdTe) are being developed to be used in covert security printing, since these NMs can be tailored to be optically active at precise wavelengths [68].

3.2 Nanomaterials Release from Paints

Performance of paints has been attracting widespread interest in recent years [69–71]. Applied in surfaces, paints undergo environmental degradation (weathering) and/or abrasion, the most common release scenarios during the lifespan of the product.

The highly opaque and bright whites of paints, for instance, are traditionally provided by TiO_2 at sizes between 200 and 300 nm (specifically rutile), and manufacturers do not claim that these products contain NPs. However, some authors have recently found that an important fraction of TiO_2 particles released from outdoors building façades to surface waters is in the range below 100 nm [72]. One of the first studies that deliberately investigated environmental release was performed by Kaegi and co-workers [69]. In this study, the presence of TiO_2 NPs in collected run-off waters from aged façade was corroborated by TEM-EDX, giving real values of mass flux of synthetic NPs into the urban environment (as high as 600 μg TiO_2/L). It should be mentioned that those TiO_2 NPs were mainly embedded in an organic binder, rather than being isolated.

The same authors investigated the release of Ag NPs (>10 nm) contained in paints exposed during 1 year to outdoor real conditions [73]. Released materials were quantified by gravimetric analysis and ICP-MS. Substantial release occurred during the first period studied (10,000 μg/L), but it drastically dropped to 1 μg/L after 8 run-off events and then it remained constant. It is worth recalling that after one year of experiment, 30 wt% of the original content of silver had been released, and interestingly TEM-EDX results suggested that the silver released form was Ag_2S.

Zuin and co-authors completed a number of studies on this topic to systematically investigate the release of different NMs from paints. The leaching of SiO_2, TiO_2 and Ag NPs was firstly studied by permanent immersion of the test specimens in water at different conditions, adopting the standardized protocol ISO 2812-2. In contrast to that reported by Kaegi in [69], small amounts of materials were collected in all cases; for SiO_2 NPs, 0.9–1.8 wt% of Si was collected with respect to the total initial Si amount. The low release rate was attributed to a better compatibilization between NMs and matrix. With respect to the nature of the material released, TEM observations indicated the presence of aggregates, particles embedded in the organic matrix and very few dispersed single SiO_2 NPs.

In a similar study, panels coated with paints containing TiO_2 NPs and weathered in a climatic chamber exhibited a much lower release of TiO_2 NPs (1.5 μg/L, total release 0.007% of the nano-TiO_2 contained in the paint) that could not be identified by TEM [74]. For that reason, in order to accelerate the release of TiO_2 and the photocatalytic degradation of the organic matrix, a UV-aged paint was extracted from its support, milled and then dispersed in water at 2 g/L. After 24 h with continuous stirring and another 24 h of settling, release amounts increased considerable up to 6 μg/L (0.025 wt% with respect to the original Ti content). It is important to recall that release observed from the NPs-free paint (i.e., with common TiO_2 pigment) after milling and stirring was much higher, around 80 μg/L. All these results clearly indicate that release of NMs from outdoors paints seems to be low.

In a follow-up study, the same authors also investigated the differences in terms of colloidal stability between pristine TiO_2 and the material released from the artificially aged paint [75]. It was concluded that the stability of the released NMs was significantly affected by the styrene-acrylic copolymer binder in the paint, rather than the surface properties of the particles. Neither pH nor salt concentration showed a significant influence on the colloidal stability of the released material.

Few more studies investigating release from aged nano-enabled coatings, other than paints, have been published. For instance, a TiO_2-based coating underwent significant loss of photocatalytic activity when aged under water flow [76]. Despite the fact that Ti could not be detected by ICP-MS (quantification limits), release of materials was confirmed by TEM analyses of collected waters and identification of samples physical degradation. However, the loss of photocatalytic activity may arise from the deactivation of TiO_2 active sites, rather than from material loss. Overall, this work suggests that the release of surface-bound NMs cannot be completely avoided. In another study, the degradation of CeO_2-based NC used for wood protection under UV light was investigated [77]. Results obtained provide insight into the degradation mechanisms and structural transformation of the citrate-coated layer and CeO_2 NPs, respectively, and gave compelling evidence that released particles can be drastically different than pristine NMs added in the original formulation.

Concerning experimental simulations of abrasion to which coatings might be exposed to during its use (e.g., sanding), some work have been conducted in a similar way as introduced in Sect. 2.2.2 for polymeric NCs, including monitoring and characterization of NMs emitted to air [56, 78, 79]. Overall, among the distinct parameters studied, such as stress strength, the results indicate that release of free NMs is rare and that they are generally released embedded in the host matrix. In accordance with the results published from weathering experiments with plastic NCs, it seems as well that the release of free NMs is favoured by prior chemical or thermal degradation [80].

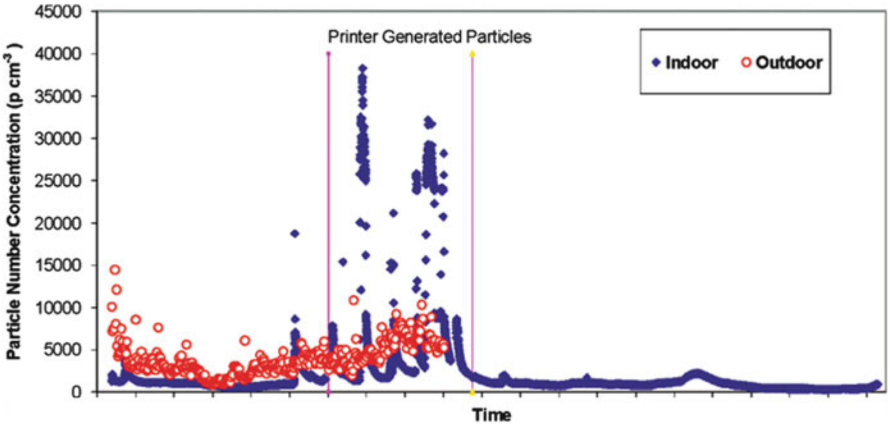

Fig. 2 Particle concentration measured by CPC indoors (office with laser printers) and outdoors for two consecutive days. Particle concentration markedly increases when printers are operating (Reprinted with permission from [81]. Copyright (2007) American Chemical Society)

3.3 *Nanomaterials Release During Printing Processes*

Since early studies provided the first evidence of high airborne particle concentrations emitted from common printers to indoor air in offices, public awareness has led to numerous investigations in this topic [65, 81, 82].

In a pioneer work, Morawska and co-workers evaluated the particle emission characteristics of 60 different commercial laser printers [81]. Surprisingly, 27% of the cases were catalogued as high particle emitters, reaching values as high as 38,000 particles/cm^3 (in the range from 0.007 to 3 μm), clearly higher than those measured outdoors (Fig. 2). Airborne particles measured had a particle count average diameter in the range of 40–60 nm, indicating a significant contribution in the number of ultrafine particles. Different parameters such as toner coverage or cartridge age were also assessed in this study.

A common encountered problem arises from the fact that it is extremely difficult to account for the individual contribution of incidental NMs (generated in the process), NMs originally present in the ink formulation and other particles originated from a different source (e.g., paper). In addition, current technology does not allow differentiating between background and NMs of interest emitted from the source. This has been partially overcome by comprehensive examination of chemical composition (EDX, ICP-MS, carbon analysis, etc.) of all the original components as well as of the emitted particles, which need to be appropriately size-fractioned for correct characterization [65]. This has led to identify distinct signs that determine a toner-based origin of the emitted particles (e.g., Sn, Ti, Fe or Mn content) [66]. Moreover, it has been demonstrated by microscopy that NMs containing TiO_2, SiO_2, Fe_3O_4 or other metals come from the original toner and are released to air, pointing out the importance of the toner formulation [65].

As mentioned above, primary toner particles have typical diameters of approximately 1 μm. It is reasonable to assume that these particles do not become aerosolized, but fragments melted in the fuser probably do [66]. In line with this, it has been hypothesized that primary airborne particles may be formed by condensation of semi-volatile organic compounds and may also include other components such as plastic housing or paper [81, 83]. Furthermore, it should be taken into account that aerosols may react and suffer modifications due to exposure to other trace pollutants or UV light.

4 Nano-Enabled Fibres

4.1 Introduction and Applications

The incorporation of NMs in the textile manufacturing industry has attracted much attention over the last decade because they can provide technical and value-added fabrics for a wide variety of applications. Desirable textile properties, such as antimicrobial or stain resistance, generally provided by the application of other production methods or conventional additives, have been improved by the use of NMs. Some examples of properties currently being investigated in the literature as well as the specific NMs involved are listed in Table 1 in the first section of this chapter.

Although literature on this subject is very extensive, the information available from the manufacturers is very scarce, which makes the degree of NMs penetration in the market very difficult to determine. The products that have clearly received the sector attention are the antimicrobial textiles, which usually contain Ag^0 NMs. Some important companies have recently marketed these products openly. However, most products with improved functional properties and claimed to contain nanotechnology are part of the company know-how.

With regard to the production methods which eventually determine the spatial distribution of NMs in final products, they strongly depend on the desired properties. Dip-pad-dry cure processes, for instance, are the most commonly used at industrial scale to deposit NMs on the surface of the final fabrics (Fig. 3), despite that this can also be accomplished by sol-gel processes or physical-vapour deposition [84]. These products are named “nanofinished textiles”, term used in the textile manufacturing industry to denote fabrics in which the nanoscale entity is incorporated after the base textile production. A vast majority of products on the market fall within this category, as post-manufacturing treatments are more simply industrially implemented.

Moreover, melt compounding and electrospinning are the methods most often employed to obtain fibres with embedded NMs. In the first case, resulting fibres are used to obtain textiles either by weaving or knitting (NC textiles), while in the second case, nanofibres can be obtained and used for further preparation of

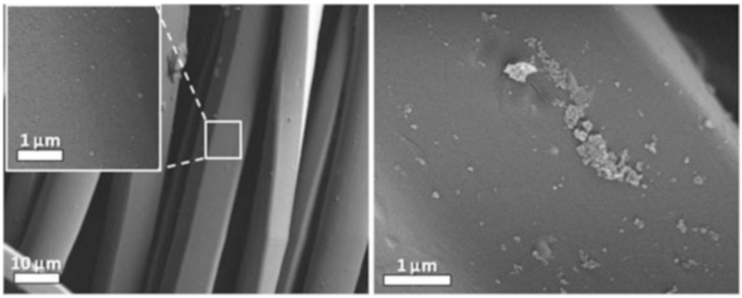

Fig. 3 Polyester fabrics containing Ag (*left*) and CuO (*right*) NPs. Particles were incorporated by dip-pad-dry cure methods at industrial scale (Courtesy of LEITAT)

nonwoven fabrics (e.g., filtration membranes). Currently, there is no technology on an industrial scale that allows nanofibres weaving [85]. Nonwoven fabrics can also be nano-additivated by surface treatment as it is done with textiles.

Another type of nano-enabled product, slightly different to conventional fabrics, is a material formed by a textile base that is coated with a polymeric NC. In this case, the element providing the functionality is the polymeric coating, not the textile itself (e.g., polyurethane or polyolefins).

4.2 Release of Nanomaterials from Textiles During Their Use

In view of the increasing concern regarding the potential risks of NMs, an increasing number of publications have focused on trying to answer the question whether NMs (mostly Ag and TiO_2) might be released from textiles, products that are available in the market since long ago [86]. A deep literature analysis reveals that the most investigated release scenarios are clothes washing and fabrics being in contact with perspiration solutions (e.g., sportswear). In both cases, environmental and human exposure is considered. It is important to remark that not only dissociated species can diffuse out of the matrix but also adsorbed particles and aggregates, which can be washed off due to mechanical abrasion forces acting or their preference for washing water (Fig. 4). These phenomena occur despite that binders are commonly added to enhance NMs and textiles affinity. Furthermore, physicochemical characterization of the product, both NMs aggregation state and evaluation of the matrix-NM bonding nature, is usually not sufficiently described by the authors.

NMs can also be released as fragments of nano-enabled textiles due to abrasion and losses occurring during the lifespan of the products. For example, it has been demonstrated that in the case of fabrics, around 10 wt% of the product is lost due to the washings during the lifespan of the product [87]. This would also apply to other textiles exposed to abrasion processes (e.g., arm-rest parts in cars or textile seats).

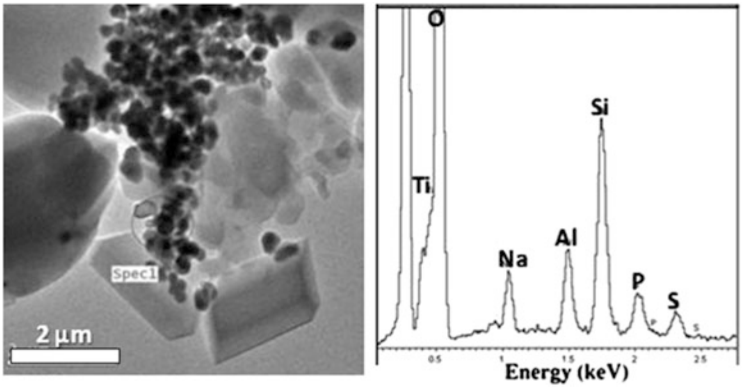

Fig. 4 Transmission electron microscopy image of released materials collected in washing solutions after one washing cycle of fabrics originally containing TiO_2 NPs. The presence of particulate matter coming from the detergent is easily observed. Elemental composition is confirmed by EDX (Courtesy of LEITAT)

Released or remaining NMs are commonly characterized by ICP-MS, combined with electron microscopy techniques coupled with EDX.

This concern has prompted a rapid rise of the studies testing simple immersion protocols [88] but also more elaborated methods trying to simulate household washing conditions [89]. Typically, the washing protocol employed is an adaptation from the ISO 105-C06:1994 for determining colour fastness in commercial and industrial laundering, which mimics real washing scenario (detergent, mild washing temperature and balls to simulate friction during the washing).

A complementary approach, based on a pull-off test (ASTM D4541), has been recently suggested by Kowal and colleagues [90]. This method consists in the evaluation of the adhesive strength of NMs binding to the fibre surfaces by applying a direct load perpendicular to the textile surface. Analysis of the adhesive tapes allows assessing both durability and adhesion strength after several washing cycles.

Comparison between nano-enabled textiles is rather difficult, due to the different natures of raw NMs, textiles (e.g., cotton or polyester) and impregnation methods (usually unknown). The studies have frequently shown that NMs release during the first washing event can be as high as 30% of the total silver amount in the textiles [91]. As expected, those samples with silver NMs embedded within the fibres have shown lower values of Ag release [92]. Nevertheless, antimicrobial activity might be suppressed due to the insufficient silver concentration on the surface.

While the release of a large fraction of ionic silver has been observed after the immersion of a nanotextile in distilled water [88], the release of particulate silver and more specifically aggregates larger than 450 nm has been reported under conditions relevant for washing [89]. In this regard, it is well known that a common washing solution contains other components that may interact with Ag, such as chloride. Interestingly, Impellitteri et al. showed that the transformation from Ag^0 to AgCl occurred in the presence of bleach [93].

As a result of the complex and wide range of possible transformations and speciation pathways of Ag, attention has been turned to investigate the chemical identity of the released particles. In this line, Lorenz et al. stated that “restriction of the Ag NPs discussion to metallic Ag NPs may miss an important aspect of Ag NPs use and release” [94]. Their results indicate that released materials from eight different textiles are significantly different between them, including Ag_2S and Ag NPs and nano-/microparticulated AgCl. This has been confirmed in other studies [92].Chemical identification is usually performed by TEM-EDX. Interestingly, the coexistence of different Ag species in textiles, before and after washing, has been demonstrated in a recent study [95], revealing that transformation of silver-based NMs on textiles during storage and before being placed into the market might occur because of air or UV exposure.

The release of Ag NPs and Ag/TiO_2 NPs to artificial sweat was assessed by immersion into a range of commercially available textiles in different types of perspiration solutions [96, 97]. These studies have concluded that the release of silver is particularly low, as total Ag amounts released ranging from 3 to 14%, while in many cases, no release was detected. However, these results were obtained after just one immersion/washing cycle, and they might be reproducing worst-case scenarios as an excess of artificial sweat is used. Kulthong et al. showed that more alkaline pH resulted in a greater release of silver [96]. In another study, it was suggested that the high chlorine content of artificial sweat had a significant effect in the rapid formation of AgCl, which was identified by TEM-EDX [97]. These studies reveal that direct consumer exposure has to be considered when evaluating potential human risk.

In line with the first immersion protocols used for textiles containing Ag NPs, the release of silver has been also studied in a large number of studies such as consumer products for children [98], wound dressing nanofibers [99] and nanofibers for membrane applications [100]. Likewise, a large number of publications on the preparation of finished nano-enabled textiles or fibres incorporate a test that would be useful to evaluate potential release/detachment/striping of NMs, especially in water-contact scenarios, though those publications do not specifically focus on NM release determination [101].

5 Nanomaterials for Healthcare and Life Science Applications

5.1 Introduction and Applications

There is a huge list of applications for NMs in the health sector. Among others, they are used as carriers for the delivery of a payload in a specific region of the body, as physical barriers against the sunrays or as anti-infective materials in operations. Compared to all other products, health and fitness products have the highest content of NMs [3]. Especially in the former field, the general trend is to produce safer-by-designed NMs. Yet, depending on its purpose, NMs can have a completely different nature and its modification may mean the loss of its functionality. Also, a huge range of NM types have been reported for healthcare applications: organic or inorganic, with a homogeneous composition or surface-functionalized, biodegradable or persistent, with a reactive surface or essentially passivated, etc.

The main characteristic of this type of nano-enabled products is that there usually is an intended human exposure. However, these exposures are considered in the product evaluations and it can be assumed that will not represent a problem for humans. However, unintentional release during their use can cause toxicity in humans (as NM can suffer modifications during the release or arrive through non-expected routes) and can impact the environment (aquatic/terrestrial systems). Apart from accidental situations, even when a product does not contain NMs, those can be generated during its use. It is accepted, for instance, that "wear-and-tear of medical devices may result in the generation of nanosized particles" [21].

The difficulty is in determining when those particles are toxic or innocuous for humans and the organisms living in the different environmental compartments. The most exhaustive document considering this issue in the area of NanoHealth is the guidance published recently by the European Commission committee SCENIHR (January 2015), which recommends a logical phased approach starting by the evaluation of NM potential release. The ISO 10993 series focuses on the characterization of medical devices and their degradation products, and ISO 14971:2007 specifies a process to identify the hazards associated with medical devices [102, 103]. However, both must be adapted and validated for NMs, as SCENIHR proposes [21]. Until now, no specific regulation or standard testing models exist for assessing exposure to NMs in healthcare or life science applications, and no risk thresholds have been defined. In addition, some authors present simple algorithms to calculate the release of NMs from consumer products (such as pharmaceuticals or cosmetics) to air, soil and water [104, 105]. Potential exposure scenarios are summarized in Fig. 5.

5.2 *Nanomaterials Administered Intentionally for Diagnostics or with a Therapeutic Purpose*

In medicine, NM dispersions (e.g., iron oxides or gold NPs for hyperthermia against cancer) or NMs embedded in matrices (e.g., dental filling composites) administered to a patient are defined as medical devices per se [21]. These formulations are designed to be intentionally administered, essentially by intravenous injection or, less frequently, by ingestion or inhalation. In these cases, because of the intentional release, large amounts of NMs interact with humans, i.e., direct contact with the bloodstream and internal tissues and the environment. The dermal/transdermal

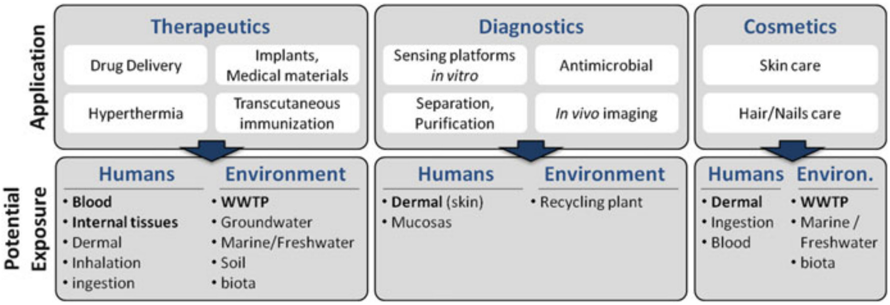

Fig. 5 Most probable NM exposure/release scenarios in the health and the cosmetic sectors

route exposes essentially the skin and the other tissues in a different degree, depending on NM penetration.

In 2014, about 200 nanotherapeutic products (85% of the nanomedical products) were reported worldwide, one third dedicated to oncology. Though none had reached the market yet, a release of some of them in the near future is envisaged, as about 120 were in clinical trials.

Currently, these applications are mainly centred on drug delivery, in vivo imaging and hyperthermia [106]. In most of these cases, NMs are designed to be administered intravenously. It can be assumed that their release is controlled and would be a percentage close to 100% in the body (a certain amount is retained in the packaging and the syringe). Nevertheless, NMs interact with the body and undergo a particular retention, clearance and degradation/transformation. Thus, biodistribution, biokinetics and excretion must be the focus to determine the fate of those NMs. Especially when NMs are not expected to degrade after its use, bioaccumulation and toxicity must be broadly assessed.

Drug delivery by inhalation, much less invasive, circumvents first-pass metabolism and avoids systemic toxicity. NMs are inhaled or released to air, and the residual volume is disposed with the packaging. Technically, only airborne particles with an aerodynamic diameter smaller than 10 μm reach significantly the pulmonary epithelium and can be retained in the lungs (respirable fraction), but the retention efficiency reaches 100% only under 2.5 μm [107]; the remaining fractions release to air or move to the gastrointestinal tract [108]. Some NMs are too small for deep lung delivery and for medical purposes must be encapsulated into microparticles. With time, the majority of NMs inhaled remain in the lung [109].

Frequently no more than 50% of the drug from the mass placed in the chamber is released as aerosol, and the fraction of NMs released to air can reach two thirds of the aerosolized solution [110]; thus, in many cases, no more than 10–15% of the prescribed dose may reach the lung. Airborne particle concentration can be reduced using more optimized devices such as jet nebulizers with a collection bag [111].

Of the nanoparticle-based therapeutics intended for clinical use, only a small percentage use the oral administration route, which releases the total NM content along the gastrointestinal tract. This route makes more feasible NM transformation and reduces NM penetration in the body, but since oral delivery is the most common method for drug administration, progress is being done to find pharmaceutical nanotechnology solutions using organic-based NMs (e.g., nanoemulsions, micelles, liposomes, solid lipid NPs), polymer-based nanocapsules or dendrimers [112, 113]. In this line, the general trend suggests an increased uptake when the size of such NMs is reduced [114, 115]. The gastrointestinal tract is a natural barrier against the systemic invasion of external agents, and for several NMs (with sizes comparable to pathogens), penetration has been demonstrated to be limited (e.g., latex, silver) [114, 116]. However, most of these NMs are contained in consumer products, and both oral uptake and continued oral exposure have proven negative effects [117]. Food companies, especially in the United States [15, 118], commercialize and work as well on the incorporation of NMs (mainly inorganic) into food and supplements to change its structure, colour and/or flavour [117, 119], though its safety has to be verified. On the contrary, for oral delivery, NMs are modified to be safe by design and reach a target tissue. Thus, in many cases, its design intentionally increases penetration through the gastrointestinal epithelium or allows its degradation at short term, avoiding bioaccumulation and release to environment.

Transdermal application of NM-based drugs is also of growing interest in medicine, as topical and transdermal drug delivery allows to maintain steady-state plasma concentrations. Though the skin epithelium, an important biological barrier, protects the body from external aggressions and from NM penetration, great controversy exists on the capability of NMs to penetrate the dermal epithelial barrier, mainly caused by the high diversity in the results published (see Sect. 5.3 for more details); according to the literature particles between 300 and 700 nm are the most prone to penetrate the skin, with an optimum size about 650 nm [120]. Pilosebaceous units are a focus of interest as well, as they can act as a reservoir of nanocarriers providing a sustained drug delivery [121]. Organic nanocarriers (e.g., liposomes, polymeric nanoparticles or dendrimers), surface-functionalized or not, are the preferred option for transcutaneous/transfollicular delivery. They can have a core-shell structure or a homogeneous composition and even respond to external stimuli such as pH, light, magnetic fields or enzymes [122]. Moreover, in most of the cases, they are biodegradable to avoid their retention in the reticuloendothelial system. In any case, after its application into the skin, NMs non-internalized transdermally are mainly released to wastewaters by two routes: attached to clothes in direct contact with the skin and washed away by water when washing or bathing. It has been demonstrated that an important fraction that ranges usually from 95 to >99% for non-targeted NMs to about 75–80% in surface-modified nanoparticles reaches the environment [123–125].

5.3 Unintended Release of Nanomaterials in Medical or Life Science Uses

Aside from the above-mentioned, NMs can be fixed to medical materials, form coatings on implants to increase biocompatibility (e.g., nanohydroxyapatite) or prevent infections (e.g., nanosilver) and be embedded to strengthen biomaterials (e.g., carbon nanotubes in a catheter wall).

The most important application of NMs in terms of production volume is as antimicrobial/anti-infective for health. Indeed textiles coated with silver or TiO_2 NPs are particularly applied to avoid proliferation of microorganisms in the skin and, thus, reduce infections. The amounts retained in the skin are essentially unknown, but several authors have reported penetration in healthy skin for both silver and TiO_2 NPs under 30 nm [126]. A special case is the electrospun polymeric nanofibrous textiles/patches for wound dressing with an antimicrobial or therapeutic effect or for controlled delivery of active ingredients [127]. Intended for skin application, these patches are expected to be removed and disposed appropriately after their use.

In the last years, electrospun polymeric nanofibers are also being proposed as scaffolds to regenerate soft (dermis, musculoskeletal tissues) or hard (bone) tissues, since they mimic the porous topography of natural extracellular matrices [127, 128]. Nanofibers can act as structural materials and as active implants simultaneously, providing a substrate for cells and releasing growth factors or other bioactive molecules. As in the previous case, these nanofibers can be made of biodegradable materials such as PLGA or PCL, to be reabsorbed once they are no longer required [129, 130]. In this application, however, nanofibers are in direct contact with internal tissues, and, although the promotion of cell proliferation has been widely demonstrated [131], the lack of data regarding nanotoxicological assessment is even more relevant.

In medical materials, nanocoatings are also used to increase specific surface area, thus improving adhesion for cell growth [132]. Used in implantable materials the permanent contact with internal tissues makes more feasible a long-term NM release, though the use of biodegradable nanocoatings is the most frequent [21, 133]. In contacting medical devices (e.g., catheters, contact lenses), silver nanocoatings with antimicrobial activity are predominant, and an acute release would be expected, if any. In both cases, nothing is known about NM release, and more exhaustive studies on tissue distribution, potential accumulation and persistence are necessary. Several authors have reported silver and TiO_2 NM accumulation (especially in lymph nodes) in rats after 17 and 90 days of intravenous administration, respectively [134, 135].

Other medical materials can release nanometric particles during their application or use, even if these are not present in the original material. For instance, handling or polishing of dental materials can generate respirable airborne NPs, increasing NP concentration in air from 10 to 45 times [136–138]. Exposure limits for these NMs have not been established yet, though as reported by the European Agency for Safety and Health at Work (EU-OSHA), they are expected to be about two orders of magnitude lower than for bulk materials [139].

Other nano-enabled materials used in medicine or life sciences, such as sensing platforms or separation/purification set-ups, contain a variable amount of NMs in different states: (a) free, dispersed in solutions for substance and cell purification as in the case of magnetic NPs, and (b) attached to surfaces for in vitro diagnostics and in point-of-care devices, even for immunochromatographic assays (e.g., gold NPs in lateral flow strips) or in nanoelectrochemical devices (e.g., micro-/nano-electro-mechanical systems or MEMS/NEMS, dip-pen/nano-lithography). For all these applications, NMs are attached and/or packed to be retained in the device or its components, and it is expected that after its use, these pieces will be disposed in special containers. Thus, no or negligible release of NMs during use is expected.

5.4 *Unintended Release of Nanomaterials in Cosmetics*

The skin, hair and nails are the target elements of the body in cosmetic treatments. In terms of production with NMs, inorganic NPs for sunscreens are the most important market, representing around 81%, followed by facial moisturizers (7.5%), foundations (5.7%) and hair colouring products (3.1%) [13]. In the cosmetic sector, NMs are generally found in suspensions (e.g., TiO_2 in sunscreens, carbon black in colourants or liposomes in anti-aging treatments), but they can occasionally be found bounded on surfaces (e.g., silver NPs in hair straighteners) [15, 140].

EU cosmetic regulation defines that prior to placing a nano-enabled product in the market, authorities must be informed about NM properties, concentration and toxicological profile and about "the reasonably foreseeable exposure conditions" [19]. It is important to mention that this normative requires ensuring a "high level of protection of human health" for every cosmetic product that contains NMs, except when used as colourants, UV filters or preservatives, which represent the most important market volume and focus of release.

5.4.1 Skin Care

Indeed, the major impact on human health and environment relative to healthcare products with NMs relies on sunscreens, one of the most widespread nano-enabled products used worldwide. For any product applied on the (healthy) skin, percutaneous penetration can occur following three routes: transcellular (the most common used by free drugs), intracellular through the lipid bilayer of the *stratum corneum* and follicular into the hair follicles. The horny layer acts as a barrier restricting strongly NM penetration but when targeted or deformable. It is well established that the major factors influencing NP dermal penetration and toxicity are size, agglomeration/aggregation, shape, crystal structure, chemical composition, surface chemistry/charge, porosity, dose, exposure time and applied formulation [141]. In addition, NMs invade deeper into hair follicles than solutions, which seems to depend on particle size (established at approximately 650 nm by Patzelt and co-workers), but not on particle composition [120]. Furthermore, negatively charged NPs interact more effectively with the skin surface, and in follicles, the sebum seems to favour the accumulation of lipid-coated NPs [142].

The majority of sunscreen preparations contain inorganic NMs as UV absorbers such as SiO_2, TiO_2, ZnO, Fe_3O_4 or Fe_2O_3. These NMs are usually applied by spraying, a procedure that can lead to exposure of the consumer lungs by inhalation [21]. About 90% of release must be expected (the remaining portion stays in the container and is disposed), as NMs are deliberately applied in the skin except if attached to surfaces for antimicrobial purposes. Thus, NMs are expected to affect the skin of the users, their lungs, but also the environment, due to direct release to sea-, fresh- and wastewaters. Keller and co-workers estimated that around 40% of NMs included in personal care products end up in landfills, 30% are released to soils, another 30% to water bodies and about 0.8% to air [140].

For inorganic NPs on the skin, Labouta and Schneider published recently a review summarizing the most relevant results [126]. Data indicate that only in about one fifth of cases (10 out of 47), penetration in healthy skin was observed at some degree, without forcing or using enhancing methods; two of these studies demonstrated penetration (of TiO_2 and CdTe quantum dots) in vivo [126]. Percutaneous penetration of nano-SiO_2 <75 nm has been as well proven [141]. With NMs such as carbon black, fullerene C60 or other mineral materials used in cosmetics, equally "released" on purpose, skin exposure and penetration should be similar. However, when used in eyeliners, nail polish or other make-up products, more tissues such as the mucosae (olfactory, GI) and eyes can be affected. The GI mucosa is as well in direct contact with TiO_2 and gold NPs in toothpastes [3]. These can retain and allow NM translocation to other tissues such as the lymph nodes, their primary recipient [143].

In beauty products, the use of nanoparticulate components has grown exponentially in the last decade. Anti-ageing and supplement (e.g., vitamins) formulations are the main applications of NMs [140], fundamentally organic nanostructures such as nanosomes (so-called liposomes), niosomes, dendrimers or solid lipid NPs, applied to the skin or hair [144]. However, these nanostructures, with a short degradation time after its application, represent a low hazard and are not included in the legal definition of an NM for cosmetics [144, 145].

5.4.2 Hair and Nail Care

Applications of NMs in this case are multiple. Inorganic NMs are immobilized in surfaces of hair irons, brushes, nail lacquers or hair dryers but also included in suspensions for hair staining. Nanoceramic metallic composites in hair dryers release the same ions and infrared wavelengths as the hairstyling irons. In addition, nanosilver particles in hairstyling and flat irons, hair dryers and nail polishes inhibit microbial growth after its use. A good example of these applications is shown by Farouk Systems Inc., a NASA spin-off that commercializes nano-enabled consumer goods [146]. Release of NMs from the mentioned product surfaces during use (in most cases heating) is feasible, with the skin of the user being the main focus of concern. In beauty treatments such as hair staining, NM suspensions (e.g., carbon black) are available in the market. In this case, however, NMs are more prone to penetrate in the hair follicles. Skin penetration of inorganic NMs has been discussed above.

Other nanotechnology-based approaches found in hair and nail care contain organic NMs, for instance, nanoemulsions to encapsulate active ingredients and carry them deeper into the hair shafts [144, 147]. In any case, once their role is performed, these NMs released into the skin and water bodies loose the nanometric structure and are supposed to represent a low hazard.

6 Research Needs

NMs have a broad range of applications. Thus, the identification of the most relevant scenarios of release is equally important to quantify and evaluate characteristics of released NMs. When release is intended such as in biocides or medical applications, technical limitations are scarce, and efforts of the scientific community can focus quickly on other issues such as to determine NM toxicity for humans and the environment. However, in most cases, release occurs accidentally and continuously over time as NMs are added to final products with a long lifetime. It is in those cases that the main difficulties arise, when real-world conditions must be simulated (lack of real vs. simulated conditions) and NMs released have to be collected for further quantification and physicochemical characterization. Furthermore, the specific characteristics of NMs require adaptation of standard procedures or new test strategies to simulate accelerated ageing of nano-enabled products, which are just starting to be designed [39] and are currently focused on mechanical degradation.

Once developed, standardization of such protocols must also be done. Maybe the most significant effort in this direction is currently being done in nanosafety projects supported by the European Commission, such as the NANoREG, though OECD, ISO and CEN are also working on this line. Nevertheless, much work remains to design valid procedures for any NM and to validate these new or adapted protocols in interlaboratory studies. Additionally, no risk threshold for NMs has been defined.

Another problem is that usually NM release is very low, so discrimination between background and NMs is limiting and challenging as well, even in laboratory assays (e.g., release from structural NCs designed for outdoor applications or from sunscreens released to the ecosphere). Most frequently NMs are composed of elements such as Si, Ti, Fe or C found widespread in nature. Even though in specific cases, such as with carbon nanotubes, electron microscopy techniques or devices specially designed [148] can be used, the issue is far from being solved.

Once a certain amount of data regarding release, physicochemical properties of NMs and its (eco)toxicity are collected, mathematical predictive modelling is a powerful tool to save efforts in determining mechanisms of potential injury and, thus, risk for new NMs and scenarios of release. In silico simulation is indeed being the focus of great attention in the last years, as it is expected to allow extrapolation from existing comparative data (i.e., physicochemical, in vitro/in vivo assays). Unfortunately, we are still far from obtaining fully functional complex models.

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References

1. Shandilya N, Le Bihan O, Morgeneyer M (2014) A review on the study of the generation of (nano)particles aerosols during the mechanical solicitation of materials. J Nanomater 2014:1–16
2. Grieger KD, Laurent A, Miseljic M et al (2012) Analysis of current research addressing complementary use of life-cycle assessment and risk assessment for engineered nanomaterials: have lessons been learned from previous experience with chemicals? J Nanoparticle Res 14:958
3. Yang Y, Westerhoff P (2014) Presence in, and release of, nanomaterials from consumer products. In: Capco DG, Chen Y (eds) Nanomater Impacts Cell Biol Med. Springer, Netherlands/Dordrecht, p 17
4. Future Markets Inc. (2014) Nanoelectronics: the global market to 2020. Future Markets Inc, Dublin
5. Global Nanocoatings Market- Industry Analysis, Size, Share, Growth, Trends, Forecast 2013-2019.
6. Future Markets Inc (2014) Nanocoatings in the medical industry, Dublin
7. Piccinno F, Gottschalk F, Seeger S, Nowack B (2012) Industrial production quantities and uses of ten engineered nanomaterials in Europe and the world. J Nanoparticle Res 14:1109
8. Mitrano DM, Motellier S, Clavaguera S, Nowack B (2015) Review of nanomaterial aging and transformations through the life cycle of nano-enhanced products. Environ Int 77:132–147
9. Sun TY, Gottschalk F, Hungerbühler K, Nowack B (2014) Comprehensive probabilistic modelling of environmental emissions of engineered nanomaterials. Environ Pollut 185:69–76
10. Kalinina A (2014) Material flow modeling, environmental concentrations and environmental risk assessment for nano silica. ETH, Zürich
11. ETP Nanomedicine (2015) Berlin, http://www.etp.nanomedicine.eu/public
12. Transparency Market Research (2013) Nanomedicine market (neurology, cardiovascular, anti-inflammatory, anti-infective, and oncology applications) – global industry analysis, size, share, growth, trends and forecast, 2013–2019. p 81
13. Keller AA, Vosti W, Wang H, Lazareva A (2014) Release of engineered nanomaterials from personal care products throughout their life cycle. J Nanoparticle Res 16:10
14. Report Buyer (2014) Global cosmeceuticals market outlook 2016. Report Buyer, London

15. Woodrow Wilson International Center for Scholars (2013) Project on emerging nanotechnologies (2013) Consumer products inventory, Blacksburg, VA, USA
16. Savolainen K, Backman U, Brouwer DH et al (2013) Nanosafety in Europe 2015–2025: towards safe and sustainable nanomaterials and nanotechnology innovations. FIOH, Helsinki
17. Hankin S, Peters S, Poland C et al (2011) Specific advice on fulfilling information requirements for nanomaterials under REACH (RIP-oN 2) – Final Project Report
18. Aitken RA, Bassan A, Friedrichs S et al (2011) Specific Advice on Exposure Assessment and Hazard/Risk Characterisation for Nanomaterials under REACH (RIP-oN 3)
19. EP (2009) Regulation (EC) No 1223/2009 of the European Parliament and of the Council of 30 November 2009 on cosmetic products. Europe
20. EP (2011) Regulation (EU) No 1169/2011 of the European Parliament and the Council of 25 October 2011 on the provision of food information to consumers. Europe
21. Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR) (2015) Final opinion on the guidance on the determination of potential health effects of nanomaterials used in medical devices. Luxembourg
22. EC (2012) Communication (COM(2012) 572 final) from the Commission to the European Parliament, the Council and the European Economic and Social Committee: Second Regulatory Review on Nanomaterials. Brussels
23. EPA (2015) Chemical substances when manufactured or processed as nanoscale materials; TSCA reporting and recordkeeping requirements. RIN: 2070-AJ54. 40 CFR Part 704. 13
24. Commission THEE (2014) Commission Implementing Regulation (EU) No 408/2014 of 23 April 2014. 2014:23–25
25. JORF (2010) Article 185. Prévention des risques pour la santé et l'environnement résultant de l'exposition aux substances à l'état nanoparticulaire. JORF n°0160 du 13 juillet 2010 p 12905, France
26. BEK (2014) BEK nr 644 af 13/06/2014. Bekendtgørelse om register over blandinger og varer, der indeholder nanomaterialer samt producenter og importørers indberetningspligt til registeret. BEK, Denmark
27. Nowack B, David RM, Fissan H et al (2013) Potential release scenarios for carbon nanotubes used in composites. Environ Int 59:1–11
28. Davim JP, Charitidis CA (eds) (2013) Nanocomposites: materials, manufacturing and engineering. De Gruyter, Berlin, Germany
29. Kumar CSSR (2010) Nanocomposites. Wiley-VCH, Weinheim, Germany
30. Twardowski TE (2007) Introduction to nanocomposite materials: properties, processing, characterization, 1st edn. DEStech Publications Inc, Lancaster
31. Rosso M (2006) Ceramic and metal matrix composites: routes and properties. J Mater Process Technol 175:364–375
32. Samal S, Bal S (2008) Carbon nanotube reinforced ceramic matrix composites–a review. J Miner Mater Charact Eng 7:355–370
33. Peigney A, Laurent C, Flahaut E, Rousset A (2000) Carbon nanotubes in novel ceramic matrix nanocomposites. Ceram Int 26:677–683
34. Zhao Z, Sun R, Xin G (2013) A review: application of nanomaterials in concrete. Appl Mech Mater 405–408:2881–2884
35. Hedayati M, Faupel F, Elbahri M (2014) Review of plasmonic nanocomposite metamaterial absorber. Materials (Basel) 7:1221–1248
36. Rohatgi P, Schultz B (2007) Lightweight metal matrix nanocomposites–stretching the boundaries of metals. Mater Matters 2:16–19
37. Camargo PHC, Satyanarayana KG, Wypych F (2009) Nanocomposites: synthesis , structure, properties and new application opportunities. Mat Res 12:1–39
38. Nowack B, Brouwer C, Geertsma RE et al (2013) Analysis of the occupational , consumer and environmental exposure to engineered nanomaterials used in 10 technology sectors. 7:1152–1156

39. Froggett SJ, Clancy SF, Boverhof DR, Canady R (2014) A review and perspective of existing research on the release of nanomaterials from solid nanocomposites. Part Fibre Toxicol 11:17
40. Ging J, Tejerina-Anton R, Ramakrishnan G et al (2014) Development of a conceptual framework for evaluation of nanomaterials release from nanocomposites: environmental and toxicological implications. Sci Total Environ 473–474:9–19
41. Petersen EJ, Lam T, Gorham JM et al (2014) Methods to assess the impact of UV irradiation on the surface chemistry and structure of multiwall carbon nanotube epoxy nanocomposites. Carbon N Y 69:194–205
42. Vilar G, Fernández-Rosas E, Puntes V et al (2013) Monitoring migration and transformation of nanomaterials in polymeric composites during accelerated aging. J Phys Conf Ser 429:012044
43. Wohlleben W, Meier MW, Vogel S et al (2013) Elastic CNT-polyurethane nanocomposite: synthesis, performance and assessment of fragments released during use. Nanoscale 5:369–380
44. Mailhot B, Morlat-Thérias S, Ouahioune M, Gardette J-L (2005) Study of the degradation of an epoxy/amine resin, 1. Macromol Chem Phys 206:575–584
45. Roger A, Sallet D, Lemaire J (1986) Photochemistry of aliphatic polyamides. 4. Mechanisms of photooxidation of polyamides 6, 11, and 12 at long wavelengths. Macromolecules 19:579–584
46. Barkoula NM, Paipetis A, Matikas T et al (2009) Environmental degradation of carbon nanotube-modified composite laminates: a study of electrical resistivity. Mech Compos Mater 45:21–32
47. Chin J, Byrd E, Embree N et al (2004) Accelerated UV weathering device based on integrating sphere technology. Rev Sci Instrum 75:4951
48. Gorham JM, Nguyen T, Bernard C et al (2012) Photo-induced surface transformations of silica nanocomposites. Surf Interface Anal 44:1572–1581
49. Kim JY, Park HS, Kim SH (2009) Thermal decomposition behavior of carbon-nanotube-reinforced poly(ethylene 2,6-naphthalate) nanocomposites. J Appl Polym Sci 113:2008–2017
50. Nguyen T, Pellegrin B, Bernard C et al (2011) Fate of nanoparticles during life cycle of polymer nanocomposites. J Phys Conf Ser 304:012060
51. Wohlleben W, Brill S, Meier MW et al (2011) On the lifecycle of nanocomposites: comparing released fragments and their in-vivo hazards from three release mechanisms and four nanocomposites. Small 7:2384–2395
52. Bello D, Wardle BL, Yamamoto N et al (2008) Exposure to nanoscale particles and fibers during machining of hybrid advanced composites containing carbon nanotubes. J Nanoparticle Res 11:231–249
53. Wohlleben W, Vilar G, Fernández-Rosas E et al (2014) A pilot interlaboratory comparison of protocols that simulate aging of nanocomposites and detect released fragments. Environ Chem 11:402
54. Hirth S, Cena L, Cox G et al (2013) Scenarios and methods that induce protruding or released CNTs after degradation of nanocomposite materials. J Nanopart Res 15:1504
55. Schlagenhauf L, Chu BTT, Buha J et al (2012) Release of carbon nanotubes from an epoxy-based nanocomposite during an abrasion process. Environ Sci Technol 46:7366–7372
56. Vorbau M, Hillemann L, Stintz M (2009) Method for the characterization of the abrasion induced nanoparticle release into air from surface coatings. J Aerosol Sci 40:209–217
57. Zhou L, Zhang Z, Xia S et al (2014) Effects of suspended titanium dioxide nanoparticles on cake layer formation in submerged membrane bioreactor. Bioresour Technol 152:101–106
58. Golanski L, Guiot A, Braganza D, Tardif F (2010) New method for the characterization of abrasion-induced nanoparticle release into air from nanomaterials. NSTI Nanotech 2010:720–723
59. Biswal M, Mohanty S, Nayak SK, Kumar PS (2013) Effect of functionalized nanosilica on the mechanical, dynamic-mechanical, and morphological performance of polycarbonate/nanosilica nanocomposites. Polym Eng Sci 53:1287–1296

60. Golanski L, Guiot A, Pras M et al (2012) Release-ability of nano fillers from different nanomaterials (toward the acceptability of nanoproduct). J Nanoparticle Res 14:962
61. Banerjee DA, Kessman AJ, Cairns DR, Sierros KA (2014) Tribology of silica nanoparticle-reinforced, hydrophobic sol–gel composite coatings. Surf Coatings Technol 260:214–219
62. Wei H, Wang Y, Guo J et al (2015) Advanced micro/nanocapsules for self-healing smart anticorrosion coatings. J Mater Chem A 3:469–480
63. Munafò P, Goffredo GB, Quagliarini E (2015) TiO_2-based nanocoatings for preserving architectural stone surfaces: an overview. Constr Build Mater 84:201–218
64. Shtykova L, Fant C, Handa P et al (2009) Adsorption of antifouling booster biocides on metal oxide nanoparticles: effect of different metal oxides and solvents. Prog Org Coatings 64:20–26
65. Bello D, Martin J, Santeufemio C et al (2012) Physicochemical and morphological characterisation of nanoparticles from photocopiers: implications for environmental health. Nanotoxicology 7:1–15
66. Barthel M, Pedan V, Hahn O et al (2011) XRF-analysis of fine and ultrafine particles emitted from laser printing devices. Environ Sci Technol 45:7819–7825
67. Kamyshny A, Magdassi S (2014) Conductive nanomaterials for printed electronics. Small 10:3515–3535
68. Haverinen HM, Myllylä R, Jabbour GE (2009) Inkjet printing of light emitting quantum dots. Appl Phys Lett 94:92–95
69. Kaegi R, Ulrich A, Sinnet B et al (2008) Synthetic TiO_2 nanoparticle emission from exterior facades into the aquatic environment. Environ Pollut 156:233–239
70. Zuin S, Massari A, Ferrari A, Golanski L (2014) Formulation effects on the release of silica dioxide nanoparticles from paint debris to water. Sci Total Environ 476–477:298–307
71. Zuin S, Gaiani M, Ferrari A, Golanski L (2013) Leaching of nanoparticles from experimental water-borne paints under laboratory test conditions. J Nanoparticle Res 16:2185
72. Weir A, Westerhoff P, Fabricius L et al (2012) Titanium dioxide nanoparticles in food and personal care products. Environ Sci Technol 46:2242–2250
73. Kaegi R, Sinnet B, Zuleeg S et al (2010) Release of silver nanoparticles from outdoor facades. Environ Pollut 158:2900–2905
74. Al-Kattan A, Wichser A, Vonbank R et al (2013) Release of TiO_2 from paints containing pigment-TiO_2 or nano-TiO_2 by weathering. Environ Sci Process Impacts 15:2186–2193
75. Botta C, Labille J, Auffan M et al (2011) TiO_2-based nanoparticles released in water from commercialized sunscreens in a life-cycle perspective: structures and quantities. Environ Pollut 159:1543–1550
76. Olabarrieta J, Zorita S, Peña I et al (2012) Aging of photocatalytic coatings under a water flow: Long run performance and TiO_2 nanoparticles release. Appl Catal B Environ 123–124:182–192
77. Auffan M, Masion A, Labille J et al (2014) Long-term aging of a CeO(2) based nanocomposite used for wood protection. Environ Pollut 188:1–7
78. Göhler D, Stintz M, Hillemann L, Vorbau M (2010) Characterization of nanoparticle release from surface coatings by the simulation of a sanding process. Ann Occup Hyg 54:615–624
79. Shandilya N, Bihan O Le, Bressot C, Morgeneyer M (2014) Evaluation of the particle aerosolization from n-TiO_2 photocatalytic nanocoatings under abrasion. J Nanomater 2014:1–12
80. Göhler D, Nogowski A, Fiala P, Stintz M (2013) Nanoparticle release from nanocomposites due to mechanical treatment at two stages of the life-cycle. J Phys Conf Ser 429:12045
81. He C, Morawska L, Taplin L (2007) Particle emission characteristics of office printers. Environ Sci Technol 41:6039–6045
82. Stephens B, Azimi P, El Orch Z, Ramos T (2013) Ultrafine particle emissions from desktop 3D printers. Atmos Environ 79:334–339
83. Morawska L, He C, Johnson G et al (2009) An investigation into the characteristics and formation mechanisms of particles originating from the operation of laser printers an

investigation into the characteristics and formation mechanisms of particles originating from the operation of laser printers. Environ Sci Technol 43:1015–1022

84. Radetić M (2013) Functionalization of textile materials with silver nanoparticles. J Mater Sci 48:95–107
85. Haydon B (2013) Nanomaterials and their Applications in Textiles – Standards Domestic Standardization for Canadian Manufacturers and Importers and International Standardization Developments Nanomaterials and their Applications in Textiles – Standards Domestic Standardization.
86. Nowack B, Krug HF, Height M (2011) 120 Years of nanosilver history: implications for policy makers. Environ Sci Technol 45:1177–1183
87. Meyer DE, Curran MA, Gonzalez MA (2009) An examination of existing data for the industrial manufacture and use of nanocomponents and their role in the life cycle impact of nanoproducts. Environ Sci Technol 43:1256–1263
88. Benn TM, Westerhoff P (2008) Nanoparticle silver released into water from commercially available sock fabrics. Environ Sci Technol 42:4133–4139
89. Geranio L, Heuberger M, Nowack B (2009) The behavior of silver nanotextiles during washing. Environ Sci Technol 43:8113–8118
90. Kowal K, Cronin P, Dworniczek E et al (2014) Biocidal effect and durability of nano-TiO_2 coated textiles to combat hospital acquired infections. RSC Adv 4:19945
91. Benn T, Cavanagh B, Hristovski K et al (2010) The release of nanosilver from consumer products used in the home. J Environ Qual 39:1875
92. Mitrano DM, Rimmele E, Wichser A et al (2014) Presence of nanoparticles in wash water from conventional silver and nano-silver textiles. ACS Nano 8:7208–7219
93. Impellitteri C, Tolaymat TM, Scheckel KG (2009) The speciation of silver nanoparticles in antimicrobial fabric before and after exposure to a hypochlorite/detergent solution. J Environ Qual 38:1528–30
94. Lorenz C, Windler L, von Goetz N et al (2012) Characterization of silver release from commercially available functional (nano)textiles. Chemosphere 89:817–824
95. Lombi E, Donner E, Scheckel KG et al (2014) Silver speciation and release in commercial antimicrobial textiles as influenced by washing. Chemosphere 111:352–358
96. Kulthong K, Srisung S, Boonpavanitchakul K et al (2010) Determination of silver nanoparticle release from antibacterial fabrics into artificial sweat. Part Fibre Toxicol 7:8
97. Von Goetz N, Lorenz C, Windler L et al (2013) Migration of Ag- and TiO_2-(Nano)particles from textiles into artificial sweat under physical stress: experiments and exposure modeling. Environ Sci Technol 47:9979–9987
98. Quadros ME, Pierson R, Tulve NS et al (2013) Release of silver from nanotechnology-based consumer products for children. Environ Sci Technol 47:8894–8901
99. Abdelgawad AM, Hudson SM, Rojas OJ (2014) Antimicrobial wound dressing nanofiber mats from multicomponent (chitosan/silver-NPs/polyvinyl alcohol) systems. Carbohydr Polym 100:166–178
100. Sichani GN, Morshed M, Amirnasr M, Abedi D (2009) In situ preparation, electrospinning, and characterization of polyacrylonitrile nanofibers containing silver nanoparticles. J Appl Polym Sci 116:1021–1029
101. Vílchez-Maldonado S, Calderó G, Esquena J, Molina R (2014) UV protective textiles by the deposition of functional ethylcellulose nanoparticles. Cellulose 21:2133–2145
102. International Organization for Standardization (2009) ISO 10993-1:2009 – biological evaluation of medical devices – part 1: evaluation and testing within a risk management process. International Organization for Standardization, Geneva, Switzerland
103. International Organization for Standardization (2007) ISO 14971:2007 – medical devices – application of risk management to medical devices. International Organization for Standardization, Geneva, Switzerland
104. Boxall ABA, Tiede K, Chaudhry Q (2007) Engineered nanomaterials in soils and water: how do they behave and could they pose a risk to human health? Nanomedicine (Lond) 2:919–927

105. Nowack B, Mueller NC (2008) Exposure modeling of engineered nanoparticles in the environment. Environ Sci Technol 42:7
106. James K, Highsmith J, Evers P (2014) Nanotechnology market – nanotechnology markets in healthcare & medicine. Drug Development & Delivery Nov–Dec:1–4
107. European Committee for standardization (1993) EN 481:1993 Workplace atmospheres – Size fraction definitions for measurement of airborne particles. European Committee for standardization, Paris, France
108. Deutsches Institut für Normung (2014) DIN EN 15051:2014 Workplace exposure – measurement of the dustiness of bulk materials. Berlin, Germany
109. Sung JH, Ji JH, Park JD et al (2011) Subchronic inhalation toxicity of gold nanoparticles. Part Fibre Toxicol 8:16
110. O'Callaghan C, Barry PW (1997) The science of nebulised drug delivery. Thorax 52(Suppl 2):S31–S44
111. Ari A (2014) Jet, ultrasonic, and mesh nebulizers: an evaluation of nebulizers for better clinical outcomes. Eurasian J Pulmonol 16:7
112. Ensign LM, Cone R, Hanes J (2012) Oral drug delivery with polymeric nanoparticles: the gastrointestinal mucus barriers. Adv Drug Deliv Rev 64:557–570
113. Mei L, Zhang Z, Zhao L et al (2013) Pharmaceutical nanotechnology for oral delivery of anticancer drugs. Adv Drug Deliv Rev 65:880–890
114. Jani P, Halbert GW, Langridge J, Florence AT (1989) The uptake and translocation of latex nanospheres and microspheres after oral administration to rats. J Pharm Pharmacol 41:809–812
115. Park E-J, Bae E, Yi J et al (2010) Repeated-dose toxicity and inflammatory responses in mice by oral administration of silver nanoparticles. Environ Toxicol Pharmacol 30:162–168
116. Park E-J, Yi J, Kim Y et al (2010) Silver nanoparticles induce cytotoxicity by a Trojan-horse type mechanism. Toxicol In Vitro 24:872–878
117. Reed RB, Faust JJ, Yang Y et al (2014) Characterization of nanomaterials in metal colloid-containing dietary supplement drinks and assessment of their potential interactions after ingestion. ACS Sustain Chem Eng 2:1616–1624
118. Friends of the Earth (2014) Tiny ingredients, big risks: nanomaterials rapidly entering food and farming. Friends of the Earth, Washington DC, USA
119. Boxall A, Chaudhry Q, Sinclair C et al (2007) Current and future predicted environmental exposure to engineered nanoparticles. Central Science Laboratory, Washington DC, USA
120. Patzelt A, Richter H, Knorr F et al (2011) Selective follicular targeting by modification of the particle sizes. J Control Release 150:45–48
121. Schleich N, Préat V (2012) Nanostructures overcoming the skin barrier: drug delivery strategies. In: Alonso MJ, Csaba NS (eds) Nanostructured biomater. Overcoming Biol. Barriers. Royal Society of Chemistry, p 13
122. Reyes-Ortega F (2014) pH-responsive polymers: properties, synthesis and applications. Smart Polymers and their Applications. Elsevier, pp 45–92
123. Gomes MJ, Martins S, Ferreira D et al (2014) Lipid nanoparticles for topical and transdermal application for alopecia treatment: development, physicochemical characterization, and in vitro release and penetration studies. Int J Nanomedicine 9:1231–1242
124. Witting M, Molina M, Obst K et al (2015) Thermosensitive dendritic polyglycerol-based nanogels for cutaneous delivery of biomacromolecules. Nanomedicine 11:1179–1187
125. Knudsen NØ, Jorgensen L, Hansen J et al (2011) Targeting of liposome-associated calcipotriol to the skin: effect of liposomal membrane fluidity and skin barrier integrity. Int J Pharm 416:478–485
126. Labouta HI, Schneider M (2013) Interaction of inorganic nanoparticles with the skin barrier: current status and critical review. Nanomedicine 9:39–54
127. Sridhar R, Venugopal JR, Sundarrajan S et al (2011) Electrospun nanofibers for pharmaceutical and medical applications. J Drug Deliv Sci Technol 21:451–468

128. Jiang T, Carbone EJ, Lo KW-H, Laurencin CT (2014) Electrospinning of polymer nanofibers for tissue regeneration. Prog Polym Sci 46:1–24
129. Zulkifli FH, Jahir Hussain FS, Abdull Rasad MSB, Mohd Yusoff M (2014) In vitro degradation study of novel HEC/PVA/collagen nanofibrous scaffold for skin tissue engineering applications. Polym Degrad Stab 110:473–481
130. Gunn J, Zhang M (2010) Polyblend nanofibers for biomedical applications: perspectives and challenges. Trends Biotechnol 28:189–197
131. Kai D, Liow SS, Loh XJ (2014) Biodegradable polymers for electrospinning: towards biomedical applications. Mater Sci Eng C Mater Biol Appl 45:659–670
132. Arsiwala AM, Raval AJ, Patravale VB (2013) Nanocoatings on implantable medical devices. Pharm Pat Anal 2:499–512
133. Puranik AS, Dawson ER, Peppas NA (2013) Recent advances in drug eluting stents. Int J Pharm 441:665–679
134. Lankveld DP, Rayavarapu RG, Krystek P et al (2011) Blood clearance and tissue distribution of PEGylated and non-PEGylated gold nanorods after intravenous administration in rats. Nanomedicine (Lond) 6:339–349
135. Geraets L, Oomen AG, Krystek P et al (2014) Tissue distribution and elimination after oral and intravenous administration of different titanium dioxide nanoparticles in rats. Part Fibre Toxicol 11:30
136. Polednik B (2014) Aerosol and bioaerosol particles in a dental office. Environ Res 134:405–409
137. Van Landuyt KL, Hellack B, Van Meerbeek B et al (2014) Nanoparticle release from dental composites. Acta Biomater 10:365–374
138. Bogdan A, Buckett MI, Japuntich DA (2014) Nano-sized aerosol classification, collection and analysis–method development using dental composite materials. J Occup Environ Hyg 11:415–426
139. Kaluza S, Balderhaar J kleine, Orthen B et al (2009) Workplace exposure to nanoparticles. European Agency for Safety and Health at Work (EU-OSHA), Spain
140. Keller A, McFerran S, Lazareva A, Suh S (2013) Global life cycle releases of engineered nanomaterials. J Nanoparticle Res 15:1692
141. Nafisi S, Schäfer-Korting M, Maibach HI (2014) Perspectives on percutaneous penetration: silica nanoparticles. Nanotoxicology 6:1–15
142. Raber AS, Mittal A, Schäfer J et al (2014) Quantification of nanoparticle uptake into hair follicles in pig ear and human forearm. J Control Release 179:25–32
143. Scientific Committee on Consumer Safety (2013) Opinion on Carbon Black (nano-form). Luxembourg
144. Little T, Lewis S, Lundquist P (2007) Beneath the skin. Investor Environmental Health Network. Falls Church, VA, USA
145. Karjomaa S (2013) Applications of nanotechnology: cosmetics. Finish Cosmetic, Toiletry and Detergent Association, Finland
146. Farouk Systems Inc (2010) Nanomaterials transform hairstyling tools. https://spinoff.nasa.gov/Spinoff2010/cg_5.html. Last visit: 16th June 2015
147. Kaplan PD (2013) Nanotechnology in dermatology. In: Nasir A, Friedman A, Wang S (eds) Nanotechnol. Dermatology. Springer, New York, p 9
148. Keller M, Kreck G, Holzapfel Y (2012) Monitoring method for carbon nanotubes (CNT): personal sampler and corresponding reading device. SENN 2012, International Congress on Safety of Engineered Nanoparticles Nanotechnologies. FIOH, Helsinki, Finland

Workplace Exposure to Process-Generated Ultrafine and Nanoparticles in Ceramic Processes Using Laser Technology

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Abstract The ceramic industry is an industrial sector, which has been growing and including innovative technologies such as laser processes. However, there is a considerable research gap within exposure assessment studies for process-generated ultrafine and nanoparticles, especially as a result of such innovations in the manufacturing processes.

This chapter addresses this issue focusing on ultrafine and nanoparticle emissions during processes in the ceramic industry with potential for unintentional nanoparticle release. The processes under study (laser sintering and ablation of ceramic tiles) have a large potential for global-scale implementation in real-world ceramic industrial facilities. Nanoparticle release mechanisms and their impact on exposure in workplace air are characterised in a selected number of release scenarios.

Keywords Ablation, Ceramic Industry, Occupational exposure, Particle release, Tile sintering

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1 Introduction

Nanoscience and nanotechnology have shown high potential for creating new opportunities and large benefits for society. However, the European Agency for Safety and Health at Work considers nanomaterials, one of the major current emerging risks at workplaces [1]. Interest is also emerging regarding airborne ultrafine particles (<100 nm) and nanoparticles (<50 nm; [2]) emitted in workplaces during industrial processes (including conventional processes, with no relation to nanotechnology and manufacturing or processing of nanomaterials). These particles, known as process-generated or non-engineered, may be similarly, to the engineered ones, potentially hazardous depending on particle properties such as size, shape, surface area and composition [3, 4].

It is commonly accepted that thermal treatments [5], combustion processes and melting [6], laser ablation [7], use of electrical equipment, soldering, welding, grinding, fracturing and abrasion activities (e.g. sanding, milling and drilling) [8–14] are typical sources with the potential to give rise to emissions of process-generated ultrafine particles and nanoparticles in workplaces [15, 16].

The growing market, fast development and spread of technologies in industrial ceramic processes (e.g. atmospheric plasma spraying, ceramic printers, laser sintering and ablation of tiles) imply that close attention should be paid to potential health risks for workers who might be exposed to airborne nanoparticles. This would comprise workers involved in conventional industrial processes and with new or developing technologies suffering from process-generated ultrafine particle and nanoparticle release. The inhalation pathway is considered the predominant route of workplace exposure and uptake [17]. As particles reach smaller diameters, they can travel deeper into the lungs [18–21]. Therefore, ceramic industries amongst others should adopt risk management strategies in order to guarantee a safe work environment [22] and obtain products with no health threats at any point of their life cycle [23]. Research on risk assessment for general nanomaterials is still not very common [24] even though it is increasing (e.g. projects MARINA, NanoReg, NanoMICEX, etc.), and reliability of adequate techniques and specific online instrumentation and standardised protocols for the detection of ultrafine particles and nanoparticles in real time is lacking [25]. Recently, progresses have been ongoing under national, European and transcontinental initiatives and projects (SIINN Eranet projects nanoIndEx and nanOximet; EU FP7 project MARINA or German BMBF projects nanoGEM and nanoCare) with the issuing of applicable guidelines.

In spite of the large evidence that workers in tile and ceramic industry are exposed to harmful airborne particles [26–29], so far, few studies are focusing on workers' exposure during the ceramic processes such as manufacture, handling and processing. Considering manufacturing processes, during machining (i.e. cutting, drilling and grinding), small-sized chips are produced, whereas during production large amounts of nanoparticles may be released to the work [30]. Voliotis et al. [31] revealed that nanoparticle emissions and subsequent exposures may reach up to particle number concentrations of 1×10^6 parts. cm^{-3} during firing processes where painting and glazing of ceramics occur. The composition of ceramics is characterised by having network formation cations (Si, B, Zr), network modifier cations (Li, Na, K, Mg, Ca, Ba, Pb, Zn) or medium cations (Al). Silica is considered the main inorganic component, although other inorganic components acting as fluxes, opacifiers or pigments can also be present. Zirconium silicate ($ZrSiO_4$), zirconium dioxide (ZrO_2), zinc oxide (ZnO), titanium dioxide (TiO_2) and tin dioxide (SnO_2) are frequently used as opacifying agents to produce opaque frits [32–35]. Amongst commercial frits, $ZrSiO_4$ is the main crystalline phase promoting opacity and whiteness in zirconium frits which are commonly designated as "white of zirconium" [32]. Other pigments are essentially composed of oxides of Al, Cu, Cr, Fe, Co, Pb, Mn and Sn [26, 35, 36].

Up to now no occupational exposure limits (OELs) have been set for any nanomaterial by the European Commission's Scientific Committee on Occupational Exposure Limits (SCOEL) or any national OEL-setting authority. The US National Institute for Occupational Safety and Health (NIOSH) [37] has proposed a recommended exposure limit (REL) of 2.4 mg m^{-3} for fine TiO_2 (defined as <2.5 μm diameter) and 0.3 mg m^{-3} for TiO_2 nanoparticles (10–100 nm) in workplace air on the basis of available toxicity data [38]. Additionally, NIOSH [39] have proposed a REL of 0.05 mg m^{-3} for respirable crystalline silica as particulate matter with a mass median aerodynamic diameter not greater than 10 μm (PM_{10}) which is also a potential occupational carcinogen [40–42]. All of these proposed REL are time-weighted average (TWA) concentrations for up to 10 h/day during a 40 h work week [37, 39]. Also, the guidance of Regulation on Registration, Evaluation, Authorisation and Restriction of Chemicals (ECHA) [43] proposed a derived no-effect level (DNELs – inhalation for workers with long-term exposure systemic effects) of 0.3 mg m^{-3} for respirable silica fumes (CAS nr. 69012-64-2) which is likely to be in the nanosized range (<100 nm). The current applicable limits for nuisance particles are established by the American Conference of Governmental Industrial Hygienists (ACGIH) [44] and Occupational Safety and Health Administration (OSHA) [45]. The OSHA [45] has set a permissible exposure limit (PEL; 8 h TWA) of 5 mg m^{-3} for the respirable fraction (PM_{10}) of particles not otherwise regulated (PNOR), whereas the ACGIH [44] believes that even biologically inert, insoluble or poorly soluble particles (particulates not otherwise specified; PNOS) may have adverse effects and suggests that airborne concentrations should be kept below the threshold limit value (TLV) 8 h TWA concentration of 3 mg m^{-3} for respirable particles (PM_{10}).

The German Institute for Occupational Safety and Health of the German Social Accident Insurance (IFA) [46] divided the biopersistent granular nanomaterials (in the range of 1–100 nm) into two groups, (i) density >6000 kg m^{-3} (Ag, Au, CeO_2, CoO, Fe, Fe_xOy, La, Pb, Sb_2O_5, SnO_2) and (ii) density <6000 kg m^{-3} (Al_2O_3, SiO_2, TiN, TiO_2, ZnO, nanoclay carbon black, C^{60}, dendrimers, polystyrene nanofibres for which asbestos-like effects are excluded), and established nano-reference values (NRV; based on IFA-benchmark levels) for these groups as 20,000 and 40,000 parts. cm^{-3}, respectively. These NRV are defined as a background corrected 8 h TWA exposure level. When dealing with process-generated nanoparticles, an assumption that the emission of the process or activity is a mix of different components and a guess for the two abovementioned groups for the supposed dominant chemical composition of the emission has to be made. In the present study, ultrafine and nanoparticles generated from ceramic processes (generally metal oxides) can be classified as biopersistent substances with a density <6000 kg m^{-3}, and thus the NRV of 40,000 parts. cm^{-3} should be applied. In general, only the pure metals have a density >6000 kg m^{-3} [16].

2 Exposure Scenarios

This chapter aims to present the results obtained during monitoring and characterisation of worker exposure to process-generated ultrafine and nanoparticles from two innovative processes with a large potential for global-scale implementation in real-world ceramic industrial facilities. This kind of processes has so far not been evaluated regarding particle emissions, to the authors' knowledge. Potential points of ceramic ultrafine particle and nanoparticle release or emission mechanisms with impact on exposure were identified:

Laser sintering of tiles: This is a novel technique with numerous advantages such as speed, temperature and enhanced durability and surface properties of structural materials [34, 47–50].

Ultrafine particle monitoring and sampling was conducted over three consecutive days, in a pilot-plant scale furnace (3 m long) in Spain, where an "in situ" melting method (tile sintering process) is applied. This process was recently developed and currently has been assessed in the framework of the networking activities of LIFE projects CERAMGLASS (LIFE11 ENV/ES/560), LASERFIRING (LIFE09 ENV/ES/435) and AIRUSE (LIFE11 ENV/ES/584). It makes use of a 350W SLAB-type high-powered CO_2 laser emitting at a wavelength $\lambda = 10.6$ μm and an optical beam steering system [50, 51].

Six conventional and frequently used types of tiles in the ceramic industry were selected. The tiles were porcelain and red clays, and in each case the tiles

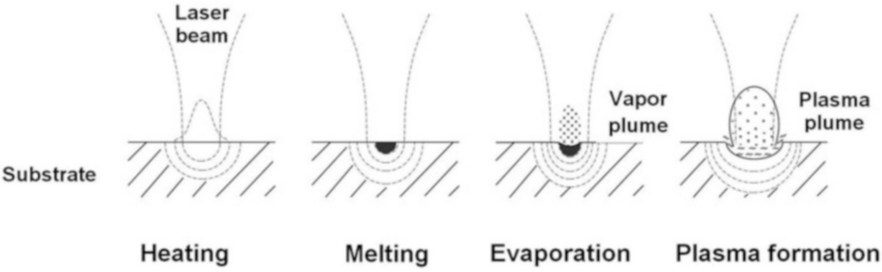


Fig. 1 Physico-chemical mechanisms occurring during sintering of ceramic tiles [80]

were raw, frit coated and frit and decoration coated. The tiles were introduced in the furnace at a constant speed (1500 mm h^{-1}) in an orthogonal direction to the laser focus. In order to avoid cracks, the samples were gradually externally heated with a resistance furnace from ambient temperature up to 850°C. Afterwards, the tiles followed the standard thermal cycles used at industrial scale, with gradually increasing temperatures which reached peak values of about 1195°C and 1115°C for porcelain and red clay tiles, respectively. Upon reaching the peak temperatures, the laser beam was introduced and directed through an optical beam steering system, which transformed the circular cross-section beam into a line measuring 1 mm in thickness and a variable width which in this case was set at 170 mm. A schematic representation of the physico-chemical processes taking place is shown in Fig. 1. This technology allows obtaining coatings of practically any oxide material on an alumina substrate [50, 51].

Laser ablation: Laser ablation is the process of expelling material from a solid surface by irradiating it with a pulsed laser beam [34, 52, 53]. The scenario makes use of the previous CO_2 laser in pulsed mode (induced laser ablation). The ablation spot can reach 1000°C, which allows the elimination of the abraded material by evaporation [34, 52]. Laser pulses can vary over a very wide range of time (milliseconds to femtoseconds) and can be precisely controlled. This technique is applied to produce engravings on the ceramic tiles. Figure 2 shows an illustration of these effects. Particle emissions during laser ablation were only assessed for one type of material (raw porcelain).

Because of their high-energy nature, these processes have a significant potential for ultrafine particle and nanoparticle release into workplace air, influencing the levels of particle concentrations and subsequently worker exposure.

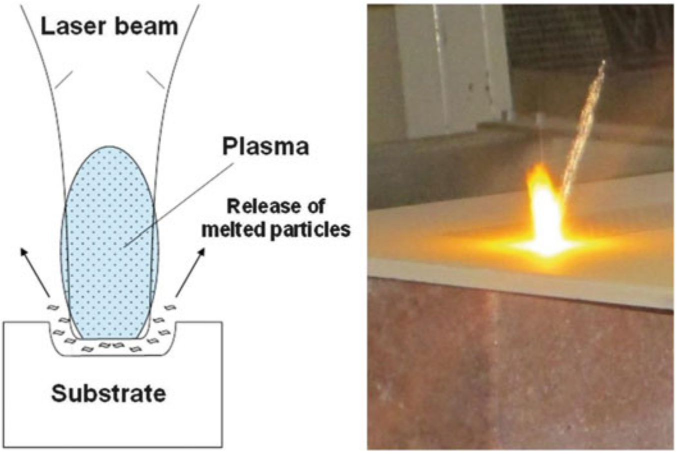


Fig. 2 Schematic representation of the ablation process (adapted from [80])

3 Measurement Strategy

Exposure assessments with special interest on airborne ultrafine particles (<100 nm in diameter) and nanosized particles (<50 nm in diameter) were conducted at pilot-plant scale. The measurement plan included measurements in workplace areas following the tiered approach as proposed by various authors [54–56].

The measurement methods employed in this study can be classified as online (size resolved/integrated and time resolved) and offline (size and time integrated) as well as methods determining particle physical and/or chemical properties.

Real-time particle measurements in the range 5 nm–20 μm were performed by means of the following instrumentation:

1. At the emission source:
    - (a) An electrical mobility spectrometer (NanoScan, SMPS TSI Inc., Model 3910, Shoreview, MN, USA; sample flow rate 0.7 L min^{1}) to measure the particle mobility size distribution in 13 channels from 10 to 420 nm mobility diameter (assuming spherical particles and charge distribution downstream of the charger). The NanoScan 3910 time resolution was 1 min.
    - (b) A water-based condensation particle counter (WCPC, TSI Model 3785, Shoreview, MN, USA; sample flow rate 1 L min^{-1}) measuring the total particle number concentration in the size range from 5 nm to 3 μm with 1 min time resolution.
2. At the breathing zone:
    - (a) An optical particle counter (OPC; Grimm Model 1.108) to measure particle mass in the range 0.3–20 μm. The sample flow rate and the sampling time

interval of the OPC were 1.2 L min^{-1} and 1 min, respectively. The particles were classified in 15 channels according to their optical diameter.

3. Simultaneously at the emission source and at the breathing zone:
   (a) Two light-scattering laser photometers (DustTrak™ II aerosol monitor TSI Model 8530; sample flow rate 3.0 L min^{-1}) to measure PM_{10}, $PM_{2.5}$ and PM_1 with 1 min time resolution. The PM values were corrected with respect to reference gravimetric values, using a high-volume reference sampler.
   (b) Two miniature diffusion size classifiers DiscMini Matter Aerosol [57] to measure total particle number, mean particle diameter and alveolar lung-deposited surface area (LDSA) concentration. The sample flow rate and the sampling time interval were 1 L min^{-1} and 1 min, respectively. According to the manufacturer, the instrument detects particles with a mode diameter between 10 and 300 nm in a concentration range between 10^3 and 10^6 parts. cm^{-3}. Particles above 700 nm were removed by a pre-impactor.

Particles emitted at the source (the furnace) were collected on 25 mm polycarbonate filters with 0.8 μm pore size. Samples were collected using cassettes (SKC Inc., USA, inlet diameter 1/8 inch) connected to SKC Leland Legacy pumps operating at 0.21 $\text{m}^3\ \text{h}^{-1}$ (3.5 L min^{-1}). The sampling periods during experiments ranged from 20 to 102 min, which correspond to air volumes sampled between 0.07 and 0.36 m^3, respectively. In addition, one accumulated sample was collected over the entire sampling period (26 h) by means of Personal Cascade Impactor Sampler (SioutasTM PCIS, SKC Inc., Eighty Four, PA, USA) [58]. Two PCIS were placed simultaneously indoor and outdoor connected to pumps operating at 9 L min^{-1}. The PCIS collected size-fractionated particles: (i) <0.25 μm, (ii) 0.25–2.5 μm and (iii) 2.5–10 μm. The collection substrates were 37 mm quartz fibre filters for the <0.25 μm (Pall) stage and 25 mm Teflon-PTFE filters for the 0.25–2.5 μm and 2.5–10 μm stages (Pall).

Mass concentrations were gravimetrically determined by pre- and post-weighting the filters on a microbalance, after they had equilibrated over 24 h periods in the weighing room under precisely controlled temperature and relative humidity conditions (23–27°C and 37–58% RH).

Additional samples were collected onto Quantifoil® gold (Au) grids with 1 μ diameter holes-4 μ separation of 200 mesh at the emission source for consecutive chemical and morphological analysis by TEM (Jeol, JEM 1220, Tokyo, Japan), coupled with an energy-dispersive X-ray (EDX) spectroscopy. TEM-Quantifoil® Au grids were attached to air sample cassettes (SKC Inc., USA, inlet diameter 1/8 inch and filter diameter 25 mm) on polycarbonate membrane filters with 0.8 μm pore size. Airflow was driven by SKC Leland Legacy pumps operating at 3.5 L min^{-1} and collection efficiency for particles was assumed to be 100%.

All the filters were acid digested by using nitric acid (HNO_3), hydrofluoric acid (HF) and perchloric acid ($HClO_4$) following the method proposed by Querol et al. [59] for the analysis of major and trace elements by means of ICP-AES (IRIS Advantage TJA Solutions, THERMO) and ICP-MS (X Series II, THERMO).

Laboratory blank filters were analysed following the same methodology. Element concentrations were blank corrected.

The average precision and accuracy for most of the elements fell under the expected analytical errors (in the range of 1–10%) and were checked by repeated analysis of NIST – 1633b (fly ash) reference material.

At the breathing zone, the sampling tube inlets were placed at the height of the nose and open mouth of the workers [60]. The distance between the furnace and the breathing zone was approximately 3 m.

The measurement strategy employed in this study allows for the calculation of the size-dependent nanoscale particle concentrations in workplaces. This is of high importance since the uptake probability of nanoparticles by inhalation is size dependent [61] and may range from around 30–40% for particles around 200 nm diameter to more than 80% for particles < 30 nm diameter [62].

4 Data Processing

Increases in particle concentrations (compared to background) were assessed with the aim to identify release mechanisms with aspects on worker exposure. The background was considered as the non-activity period not immediately preceding the start of activity [60]. However, it is important to take into account that this approach assumes background concentrations to be constant which may not always be the case [62].

Workplace air particle concentrations deriving from process-related particle release were calculated as the difference between the measured effective particle concentrations at the workplace during the work activity (WA) and the background (BG) registered concentrations:

$$\text{Process-related workplace particle concentration} = \text{WA} - \text{BG}. \tag{1}$$

This approach is similar to the description in Asbach et al. [56] and Kaminski et al. [62].

If particle concentrations in workplace air are higher than the background, it should be evaluated whether this increase is statistically significant. According to Asbach et al. [56], the difference is considered statistically significant if the mean particle concentration in workplace air is higher than the BG concentrations plus three times the standard deviation of the BG concentration:

$$\text{Significant Release} > \text{BG} + 3.\sigma_{\text{BG}}, \tag{2}$$

where σ_{BG} is the standard deviation of the BG. This means that if the ratio

$$\frac{\text{Process-related workplace particle concentration}}{3.\sigma_{\text{BG}}} > 1, \quad (3)$$

then particle release should be considered as significant.

The cumulative worker exposure for an 8 h working shift was calculated as follows:

$$\text{Worker exposure} = \frac{\sum C_i t_i}{\sum_i^n t_i} = \frac{C_1 t_2 + C_2 t_2 + \ldots C_n t_n}{8} - \text{BG}, \quad (4)$$

where C_i is the concentration during any period of time t_i; $\sum_i^n t_i$ is the duration of the work shift which was considered as 8 h.

The value of worker exposure shall not exceed the 8 h TWA specified in current applicable limits by regulations.

5 Ultrafine Particle and Nanoparticle Release During Laser Sintering

The time series of particle number concentrations, measured at the emission source (the furnace for sintering processes) and in the breathing zone, from porcelain and red clay tile raw (#1 and #4), frit coated (#2 and #5) and frit and decoration coated (#3 and #6) are shown in Fig. 3. In a previous work, [63] studied particle emission mechanisms during tile sintering and observed that tile sintering at industrial scale is a particle-generating process, characterised by major ultrafine particle and nanoparticle emissions reaching up to 2.4×10^7 parts. cm^{-3} at the emission source (Fig. 3). Fonseca et al. [63] concluded that particle emissions are linked to raw tile chemical composition and to two kinds of processes: (a) thermal-induced emissions during melting of the tile surface and (b) new particle formation processes from gaseous emissions by nucleation events (nanoparticles <30 nm in diameter being formed; [64]), before the laser application. In the present work, worker exposure to ultrafine particles and nanoparticles derived from the particle emission mechanisms described by Fonseca et al. [63] was assessed. As evidenced by Fig. 3, exposure concentrations in the breathing zone were high and strongly linked to the emission mechanisms. Both emissions and exposure to ultrafine particles and nanoparticles seemed to be independent of the laser treatment, as they were mainly process temperature dependent.

Table 1 summarises the mean and maximum exposure concentrations obtained in terms of number and alveolar lung-deposited surface area (LDSA), as well as the significance level of particle number concentration and the mean particle diameter

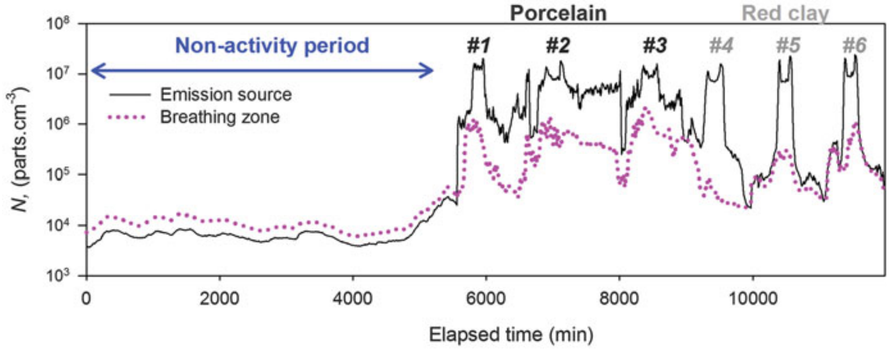


Fig. 3 Time series of particle number concentrations (range of 10–700 nm) measured simultaneously at emission source and breathing zone

Table 1 Average and maximum (in parenthesis) particle number concentrations, particle diameter and significance of exposure (range 10–700 nm) during tile sintering measured in the breathing zone and background. Mean values corresponding to each sintering process, approximately 1.5 h. Maximum values are 1 min means

Material	N_{total} (parts. cm^{-3})	D_p (nm)	LDSA (μm^2 cm^{-3})	Ratio $= \frac{\text{Released } N_{\text{total}}}{3.\sigma_{BG}}$ [a]
#1: Raw porcelain	3.0×10^5 (1.2×10^6)	18 (26)	277 (1,547)	11
#2: Porcelain with frit coated	5.6×10^5 (1.4×10^6)	13 (28)	371 (1,686)	21
#3: Porcelain with frit and decoration coated	8.0×10^5 (2.3×10^6)	16 (29)	687 (2,271)	31
#4: Raw red clay	7.5×10^4 (4.7×10^5)	27 (36)	69 (223)	2
#5: Red clay with frit coated	1.1×10^5 (3.1×10^5)	26 (38)	115 (229)	4
#6: Red clay with frit and decoration coated	2.7×10^5 (1.2×10^6)	19 (35)	213 (551)	10
Background[b]	1.3×10^4 (6.0×10^4)	34 (42)	21 (45)	–

[a] Calculated by Eqs. (1) and (3)

[b] Corresponding to non-activity period; $3.\sigma_{BG} = 2.6 \times 10^4$ parts cm^{-3}

measured at the worker breathing zone during tile sintering and during the non-activity period.

Over the 1.5 h periods during which each of the tiles underwent the thermal treatment, major nanoparticle emissions were registered at the emission source in the furnace which resulted in increased concentrations in the breathing zone (Fig. 3). On average, mean and maximum N 1 min exposure concentrations were 1–2 orders of magnitude higher than background exposure levels. Mean particle diameters were 13–27 nm, as opposed to 34 nm in background air and larger than the mean diameters measured during release at emission source (8–18 nm), as expected due to particle transport across the plant (Table 1). As a result, this initial assessment evidences the large potential for nanoparticle exposure of tile sintering in furnaces, as well as the small and potentially health-relevant diameter of the particles to which the workers are exposed. Besides the total particle concentration monitored in the breathing zone, Table 1 also lists the ratio according Eq. (3). This ratio indicated and confirmed statistically significant exposure increases during the sintering process in the workplace since the process-related workplace particle concentration (calculated by Eq. 1) was always higher than $3.\sigma_{BG}$ (2.6×10^4 parts. cm^{-3} for particles in the range of 10–700 nm).

The highest nanoparticle exposure concentrations were registered during porcelain tile sintering and, in particular for material #3 (frit and decoration coated), reaching a maximum of 2.3×10^6 parts. cm^{-3} (particle mean diameter = 16 nm). Maximum nanoparticle concentrations during sintering of a similarly coated material (#6, frit- and decoration-coated red clay) were lower by a factor of 1.9, thus suggesting that majority of the nanoparticles originates from the base of the tiles, as opposed to the coating materials. On average, exposure to nanoparticles was higher during porcelain sintering (5.5×10^5 parts. cm^{-3}) when compared to red clay (1.5×10^5 parts. cm^{-3}). This is an especially relevant finding for the tile industry, given that the demand for porcelain tiles is currently increasing in the global ceramic market due to aesthetic reasons. Regarding mean particle diameter, nanoparticles generated during red clay sintering were on average coarser (24 nm) in the breathing zone than during porcelain tile sintering (16 nm).

The results from this study are comparable with the range found in other ceramic process-generated ultrafine and nanoparticle exposure studies [4, 5, 9, 12, 31, 65–68]. For example, according Voliotis et al. [31], during firing processes of ceramics in a kiln of a traditional small-sized pottery studio, the average particle number concentration of the background air was approximately 9×10^3 parts. cm^{-3}, while in this study concentrations of 1.3×10^4 parts. cm^{-3} were found. Furthermore, they also reported that the average particle number concentration during bisque firing was 1.6×10^5 parts. cm^{-3}, whereas the respective value during glaze firing was 2.5×10^5 parts. cm^{-3}. The respective concentrations of particles having diameters smaller than 100 nm were 1.4×10^5 and 2.5×10^5 parts. cm^{-3}, while the average concentration in this study during sintering processes for particles <300 nm as mode diameter was 3.3×10^5 parts. cm^{-3}.

The alveolar LDSA of the nanoparticles emitted during tile sintering and measured in the breathing zone was significantly larger than in background air (corresponding to non-activity period). Background air LDSA concentrations were 21 μm^2 cm^{-3} and they increased by a factor ranging from 3 to 33 in the breathing zone (Table 1), thus indicating important exposure levels for workers. LDSA concentrations were higher during porcelain sintering than during red clay sintering. In terms of average values, sintering of frit- and decoration-coated porcelain tile exhibited the highest mean value (6.9×10^2 μm^2 cm^{-3}).

A relatively similar pattern was observed for particle mass (Table 2) and the workers exposure should be also considered as exposure on a statistically significant level (Eq. 2); Significant Release > BG + $3.\sigma_{BG}$). The highest PM_{10} emissions were

Table 2 Average and maximum (in parenthesis) PM measured at breathing zone during tile sintering (from materials #1 to #6) and background concentrations

Material	PM_1 (μg m^{-3})	$PM_{2.5}$ (μg m^{-3})	PM_{10} (μg m^{-3})
#1: Raw porcelain	6.1 (8.9)	7.3 (12.0)	13.2 (19.9)
#2: Porcelain with frit coated	5.9 (7.8)	7.0 (10.4)	12.5 (21.4)
#3: Porcelain with frit and decoration coated	8.2 (12.8)	10.7 (18.3)	17.0 (26.2)
#4: Raw red clay	6.5 (8.0)	8.0 (10.5)	13.8 (16.7)
#5: Red clay with frit coated	7.3 (9.1)	9.3 (12.4)	15.7 (19.4)
#6: Red clay with frit and decoration coated	7.7 (13.8)	10.0 (20.2)	16.3 (28.5)
Background[a]	5.3 (5.9)	5.9 (7.0)	10.8 (12.8)

[a] Corresponding to non-activity period; σ_{BG} for PM_1, $PM_{2.5}$ and PM_{10} were 0.1, 0.2 and 0.3 μg m^{-3}, respectively

generated during sintering of frit- and decoration-coated porcelain tiles (material #3), although followed closely by frit- and decoration-coated red clay (material #6). On average, tile sintering increased particle mass concentrations with respect to background air by a factor of 1.3 for PM_1, 1.5 for $PM_{2.5}$ and 1.4 for PM_{10}. However, these ratios varied as a function of the tiles. For example, PM_1, $PM_{2.5}$ and PM_{10} in the case of raw porcelain (material #1) equalled 1.2, 1.2 and 1.2 times the background concentrations, and for frit- and decoration-coated porcelain (material #3), these ratios were 1.5, 1.8 and 1.6, respectively, showing a higher emission of coarse particles. On the other hand, for the remaining materials, higher emissions of submicrometer particles were observed.

The results concerning the particle mass concentrations presented here are considerably lower than those found in production plants of nanostructured TiO_2 and Al_2O_3 particles. Kaminski et al. [62] measured an average PM_{10} exposure during the work activities varying from 48 to 1330 μg m^{-3}, whereas the results of PM_{10} presented here showed levels of 12.5 to 17 μg m^{-3}.

The TEM analysis shows a remarkable number of ultrafine spherical nanoparticles (mostly <100 nm) in workplace air (Fig. 4) which may be interpreted as portions of melted material involved in melting processes at a high temperature under the laser beam. Chemical analysis by EDX showed that the ultrafine particles mostly contained traces of Zn, Cr and Fe due to the extensive use of these substances as opacity and pigmentation agents in ceramic tiles [35, 36]. These observations are in agreement with the findings reported by Jordán et al. [69] and Sanfeliu et al. [70] where tracers of atmospheric emissions of ceramic industries were sampled as spherical particles.

Mass concentrations of $PM_{<0.25}$, $PM_{0.25\text{-}2.5}$ and $PM_{2.5\text{-}10}$ collected in indoor air (aggregated for all of the sintering processes, from #1 to #6) were 43.1 μg m^{-3}, 5.3 μg m^{-3} and 4.8 μg m^{-3}, respectively. These concentrations were 4.3, 1.3 and 1.7 times higher than those obtained simultaneously outdoors, respectively. Indoor/outdoor concentration ratios (I/O) were >1 for most elements and size fractions, but they were highest for elements in $PM_{<0.25}$ (see Fig. 5). These results confirm that

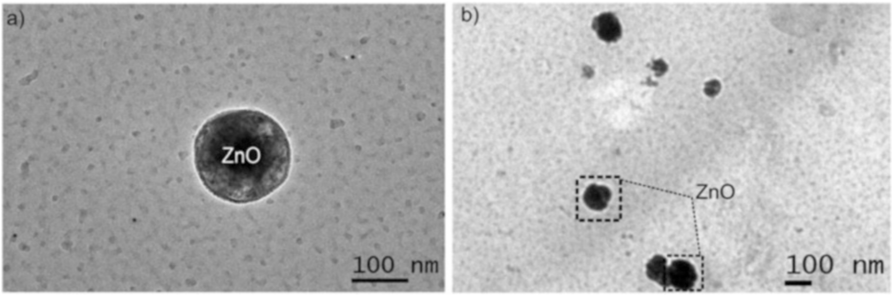


Fig. 4 TEM images of nanoparticles collected in workplace air during: (**a**) sintering of porcelain with frit coated; (**b**) sintering of red clay frit coated. Corresponding identified particles by EDX are shown in each figure

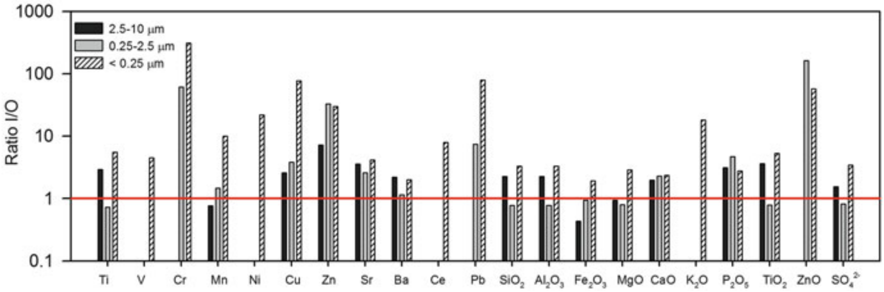


Fig. 5 I/O ratios of major and trace elements for size-fractionated particles (<0.25, 0.25–2.5 and 2.5–10 µm). I/O ratios above and below the *red horizontal line* indicate the predominance of indoor and outdoor sources, respectively

the effect of major indoor sources, i.e. emissions from sintering processes, generate mostly fine particles. It should be stated that recent unpublished work by the authors suggests that the cutoff at 250 nm of the sampler used is not sufficiently precise and that coarser particles (<1 µm) may have been collected in this size fraction.

I/O ratios were especially high for typical tracers of components in $PM_{<0.25}$ used in the mix of frits and pigments in tile decoration such as Cr, Mn, Ni, Cu, Ce and Pb ([71]; Sánchez [72]). Concerning $PM_{0.25\text{-}2.5}$, the main species with I/O ratios >1 were P_2O_5 and ZnO. Zn is very often used in frit and enamel formulas [35, 36]. Finally, coarse particles ($PM_{2.5\text{-}10}$) showed a larger occurrence of I/O ratios >1 for Ba. I/O ratios <1 indicate the predominance of outdoor sources or particle losses and evaporation processes indoors. This was the case for certain crustal elements of outdoor origin such as Al, Ti and Fe, indicating that their origin is mainly linked to African dust or to traffic resuspension of road dust [73]. As expected, secondary inorganic aerosols such as NO_3^- also showed ratios <1 in the accumulation mode due to losses through infiltration [74, 75]. The highest concentrations of potentially harmful metals measured in workplace air (mainly Zn, Pb, Cu, Cr, As and Tl) were found in the ultrafine fraction <250 nm. These results have direct implications for the ceramic industry, given the current increasing global demand for porcelain tiles and the similarly decreasing demand for red clay tiles. This would imply increasing exposures to nanoparticles of lower diameters (<30 nm) in ceramic industrial plants.

To sum up, it can be concluded that ultrafine and nanosized airborne particles were generated and emitted into workplace air during sintering process on a statistically significant level ($> \mathrm{BG} + 3.\sigma_{\mathrm{BG}}$ [56]). When comparing exposure levels to the exposure limits available in current regulations, according to IFA [46], the ultrafine and nanoparticles generated in this workplace may be estimated to have in general a density of <6000 kg m^{-3} which is assigned a nano-reference value (NRV) of 40,000 parts. cm^{-3}. Comparing the average ultrafine particle and nanoparticle concentrations at the breathing zone during the activity period in this study with the NRV, it can be concluded that in the setting under study, workers would be exposed to concentrations above the NRV, since their 8 h TWA would be 2.8×10^5 parts. cm^{-3} (worst-case scenario calculated by Eq. (4) considering an equivalent worker exposure of 7 h working shift during sintering activity and 1 h working shift during non-activity period). In terms of mass, current regulations set a 3 mg m^{-3} limit (8 h TWA; [44]), for the total respirable fraction, which would not have been exceeded during sintering conditions given that the PM_1, $\mathrm{PM}_{2.5}$ and PM_{10} for 8 h TWA would be 1.4, 2.3 and 3.3 μg m^{-3}, respectively.

As a result, it would be advisable to implement preventive and protective actions (e.g. introduction of exhaust fume extraction) in ceramic industries using tile sintering in order to reduce worker exposure to acute particle release events.

6 Ultrafine and Nanoparticle Release During Tile Ablation

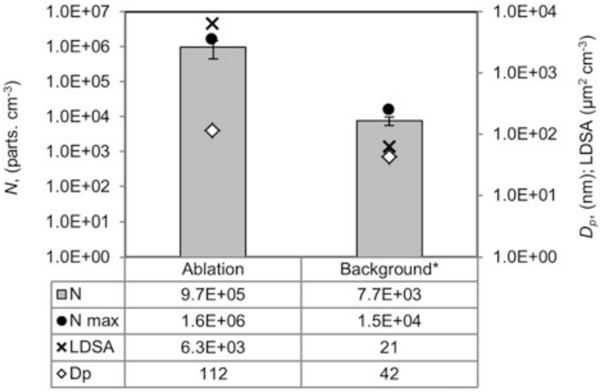
By using the same measurement strategy and data interpretation as above, Fig. 6 and Table 3 show the results from the ablation of raw porcelain tiles. This assessment was performed only in the breathing zone.

Results from Fig. 6 and Table 3 show that exposure to particles generated during ablation process were higher in terms of mass ($\mathrm{PM}_1 = 49$, $\mathrm{PM}_{2.5} = 84$ and $\mathrm{PM}_{10} = 103$ μg m^{-3}) than during sintering. Furthermore, the particle size was highest showing a mean diameter of 112 nm. This means that the ceramic tile ablation process produces greater particle mass emissions compared with the sintering process. These observations were expected during ablation because it is a mechanical process (as opposed to a thermal process).

The average PM_1 obtained during ceramic ablation process (49 μg m^{-3}) is lower than 800 and 860 μg m^{-3} obtained during drilling and cutting of hardened concrete, respectively [68]. Also, the average particle number concentration after subtracting the background from the particle number concentration during the ablation activity was found to be in the same order of magnitude during drilling and cutting concrete activities (2.1 and 6.1×10^5 parts. cm^{-3}, respectively).

The alveolar LDSA concentrations during tile ablation (Fig. 6) exceeded the levels recorded during sintering, reaching an average value of 6.3 x 10^3 $\mu\mathrm{m}^2$ cm^{-3}.

Fig. 6 Average, maximum and standard deviations (error bars) of particle number concentrations, particle diameter and LDSA measured during tile ablation in the breathing zone and background air (range 10–420 nm). Mean values corresponding to ablation process, approximately 20 min in duration. Maximum values are 1 min means



	Ablation	Background*
▨N	9.7E+05	7.7E+03
●N max	1.6E+06	1.5E+04
×LDSA	6.3E+03	21
◇Dp	112	42

*Corresponding to non-activity period

Table 3 Calculated mean particle concentrations (according to Eq. 1) and corresponding standard deviation (±σ) during the WA and BG for particles below and larger than 100 nm

Material	Released $N_{<100\ \mathrm{nm}}$ (parts. cm^{-3})	Released $N_{>100\ \mathrm{nm}}$ (parts. cm^{-3})	Released PM_1 (μg m^{-3})	Released $\mathrm{PM}_{2.5}$ (μg m^{-3})	Released PM_{10} (μg m^{-3})
Ablation	$2.8 \times 10^5 \pm 1.8 \times 10^5$	$6.8 \times 10^5 \pm 4.1 \times 10^5$	49 ± 29	84 ± 50	103 ± 60
Background[a]	$7.2 \times 10^3 \pm 2.7 \times 10^3$	$5.1 \times 10^2 \pm 3.0 \times 10^2$	5.3 ± 0.1	5.9 ± 0.2	10.8 ± 0.3

[a] Corresponding to non-activity period

Monitored levels of LDSA, in both processes but especially during ablation processes, were significantly higher than outdoor levels registered in major European cities such as Dusseldorf, Germany (30–45 μm^2 cm^{-3}) [76]; Lisbon, Portugal (35–89 μm^2 cm^{-3}) [77, 78]; and Barcelona, Spain (37 ± 26 μm^2 cm^{-3}) [79].

The particle number size distributions (between 10 and 420 nm, measured by the NanoScan instrument; Fig. 7) showed that the laser ablation of porcelain tiles produced a bimodal curve, with mode values 10–50 nm and 50–420 nm, with a clear prevalence of coarser particles (>100 nm), whereas a prevalence of particles <50 nm was observed in the background. The mean particle diameters produced from ablation process were mainly particles between 65 and 200 nm (for >90% of the particles) in number.

The corresponding TEM samples (Fig. 8) show a remarkable number of spherical particles where aggregates of particles in the nanosized range are observed. This is expected to occur due to the fact that laser engraving induces phase transitions, causing catastrophic break down of the original material [34].

Chemical analysis by TEM/EDX showed that the main inorganic component released is SiO_2 although other components acting as fluxes, opacifiers or pigments such as Cu, Cr, Ti, Fe, P and Ca are also present in the breathing zone [35, 36].

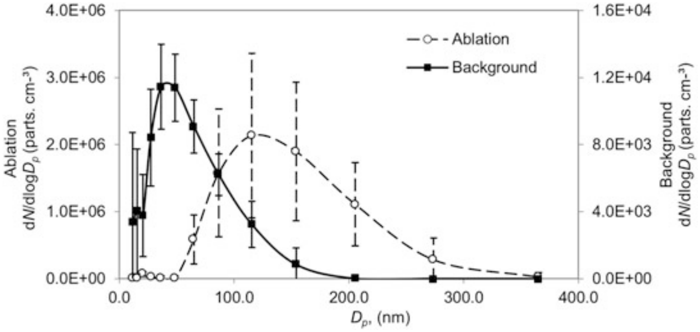


Fig. 7 Average background (*continuous line*) and average measured size distributions of particles during porcelain ablation (*dashed line*) including normal standard deviations (± σ)

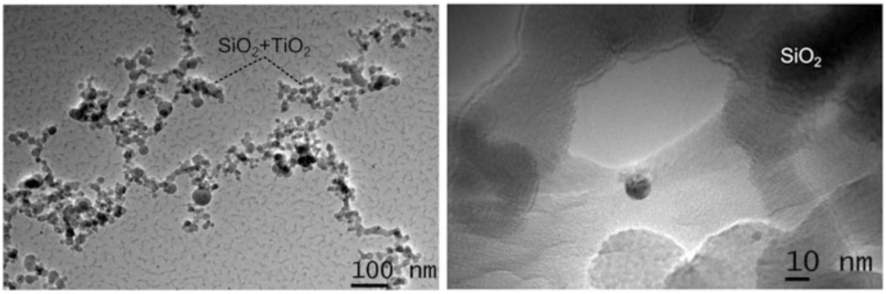


Fig. 8 TEM images of nanoparticles collected in indoor air during ablation of raw porcelain. Corresponding identified particles by TEM/EDX are shown in each figure

These results evidenced ablation ratios (Eq. 3) greater than 1 showing significant particle releases and exposures to particles <100 nm.

Similarly to the sintering activities described above, the ablation process generates particle emissions which result in exposure concentrations lower than the 3 mg m^{-3} limit set by ACGIH [44]. Due to the short duration of this activity (20 min), TWAs cannot be calculated.

Once again preventive measures against the release would be advisable.

7 Summary

The results from this study evidence the risk of occupational exposure to ultrafine particles and nanoparticles during high-energy laser processes in the ceramic industry. Overall, particles in the nanoparticle size range (<100 nm diameter) are released into workplace air. Hence, the development of mitigation strategies and systematic approaches towards better identifying the processes and/or materials are recommended to enable risk assessments and reduce worker exposure.

References

1. EU-OSHA (2009) Workplace exposure to nanomaterials. European Agency for Safety and Health at Work, Bilbao
2. Hirano S (2009) A current overview of health effect research on nanoparticles. Environ Health Prev Med 14(4):223–225
3. Scenihr (2009) Scientific committee on emerging and newly identified health risks. Risk assessment of products of nanotechnologies. European Commission, Health & Consumers DG, Directorate C: Public Health and Risk Assessment. http://ec.europa.eu/health/ph_risk/risk_en.htm. Accessed 2 Apr 2015
4. Van Broekhuizen P, Van Veelen W, Streekstra W-H, Schulte P, Reijnders L (2012) Exposure limits for nanoparticles: report of an international workshop on nano reference values. Ann Occup Hyg 56(5):515–524. doi:10.1093/annhyg/mes043
5. Evans DE, Ku BK, Birch ME, Dunn KH (2010) Aerosol monitoring during carbon nanofiber production: mobile direct-reading sampling. Ann Occup Hyg 54(5):514–531. doi:10.1093/annhyg/meq015
6. Donaldson K, Tran L, Jimenez L, Duffin R, Newby D, Mills N, MacNee W, Stone V (2005) Combustion-derived nanoparticles: a review of their toxicology following inhalation exposure. Part Fibre Toxicol 2(1):10
7. Barcikowski S, Bärsch N, Ostendorf A (2007) Generation of nano-particles during laser ablation – risk assessment of non-beam hazards during laser cleaning. In: Nimmrichter J, Kautek W, Schreiner M (eds) Lasers in the conservation of artworks, vol 116. Springer, Berlin Heidelberg, pp 631–640
8. Szymczak W, Menzel N, Keck L (2007) Emission of ultrafine copper particles by universal motors controlled by phase angle modulation. J Aerosol Sci 38(5):520–531. doi:10.1016/j.jaerosci.2007.03.002
9. Evans DE, Heitbrink WA, Slavin TJ, Peters TM (2008) Ultrafine and respirable particles in an automotive grey iron foundry. [Research Support, Non-U S Gov't]. Ann Occup Hyg 52(1):9–21
10. Peters TM, Elzey S, Johnson R, Park H, Grassian VH, Maher T, O'Shaughnessy P (2009) Airborne monitoring to distinguish engineered nanomaterials from incidental particles for environmental health and safety. J Occup Environ Hyg 6(2):73–81
11. Koponen IK, Jensen KA, Schneider T (2009) Sanding dust from nanoparticle-containing paints: physical characterisation. J Phys 151(1):012048
12. Pfefferkorn FE, Bello D, Haddad G, Park J-Y, Powell M, McCarthy J, Bunker KL, Fehrenbacher A, Jeon Y, Virji MA, Gruetzmacher G, Hoover MD (2010) Characterization of exposures to airborne nanoscale particles during friction stir welding of aluminum. Ann Occup Hyg 54(5):486–503. doi:10.1093/annhyg/meq037
13. Göhler D, Stintz M, Hillemann L, Vorbau M (2010) Characterization of nanoparticle release from surface coatings by the simulation of a sanding process. Ann Occup Hyg 54(6):615–624. doi:10.1093/annhyg/meq053
14. Wohlleben W, Brill S, Meier MW, Mertler M, Cox G, Hirth S, von Vacano B, Strauss V, Treumann S, Wiench K, Ma-Hock L, Landsiedel R (2011) On the lifecycle of nanocomposites: comparing released fragments and their in-vivo hazards from three release mechanisms and four nanocomposites. Small 7(16):2384–2395
15. Borm P, Robbins D, Haubold S, Kuhlbusch T, Fissan H, Donaldson K, Schins R, Stone V, Kreyling W, Lademann J, Krutmann J, Warheit D, Oberdorster E (2006) The potential risks of nanomaterials: a review carried out for ECETOC. Part Fibre Toxicol 3(1):11
16. Van Broekhuizen P (2012) Nano matters: building blocks for a precautionary approach, PhD thesis. www.ivam.uva.nl/?nanomatters
17. Schmoll LH, Elzey S, Grassian VH, O'Shaughnessy PT (2009) Nanoparticle aerosol generation methods from bulk powders for inhalation exposure studies. Nanotoxicol 3(4):265–275. doi:10.3109/17435390903121931

18. Oberdorster G (2001) Pulmonary effects of inhaled ultrafine particles. Int Arch Occup Environ Health 74(1):1–8
19. Hoet PH, Bruske-Hohlfeld I, Salata OV (2004) Nanoparticles – known and unknown health risks. J Nanobiotechnology, 2(1):12
20. Heal MR, Kumar P, Harrison RM (2012) Particles, air quality, policy and health. Chem Soc Revi 41(19):6606–6630. doi:10.1039/c2cs35076a
21. Weichenthal S (2012) Selected physiological effects of ultrafine particles in acute cardiovascular morbidity. Environ Res 115:26–36
22. Hameri K, Lahde T, Hussein T, Koivisto J, Savolainen K (2009) Facing the key workplace challenge: assessing and preventing exposure to nanoparticles at source. Inhal Toxicol 1:17–24
23. Friedrichs S, Schulte J (2007) Environmental, health and safety aspects of nanotechnology—implications for the R&D in (small) companies. Sci Technol Adv Mater 8(1–2):12–18. doi:10.1016/j.stam.2006.11.020
24. Maynard AD (2007) Nanotechnology: the next big thing, or much ado about nothing? Ann Occup Hyg 51(1):1–12. doi:10.1093/annhyg/mel071
25. Savolainen K, Backman U, Brouwer B, Fadeel B, Fernandes T, Kuhlbusch T, Landsiedel R, Lynch I, Pylkkanen L (2013) Nanosafety in Europe 2015–2025: towards safe and sustainable nanomaterials and nanotechnology innovations. Finnish Institute of Occupational Health. http://www.ttl.fi/en/publications/electronic_publications/pages/default.aspx
26. Taylor JR, Bull AC, Ceramics IO (1986) Ceramics glaze technology. Institute of Ceramics, Pergamon
27. Bache CA, Lisk DJ, Scarlett JM, Carbone LG (1991) Epidemiologic study of cadmium and lead in the hair of ceramists and dental personnel. J Toxicol Environ Health 34(4):423–431
28. Hirtle B, Teschke K, van Netten C, Brauer M (1998) Kiln emissions and potters' exposures. [Research Support, Non-U S Gov't]. Am Ind Hyg Assoc J 59(10):706–714
29. Monfort E, García-Ten J, Celades I, Gazulla MF, Gomar S (2008) Evolution of fluorine emissions during the fast firing of ceramic tile. Appl Clay Sci 38(3–4):250–258. doi:10.1016/j.clay.2007.03.001
30. Gandra J, Miranda R, Vilaça P, Velhinho A, Teixeira JP (2011) Functionally graded materials produced by friction stir processing. J Mater Process Technol 211(11):1659–1668. doi:10.1016/j.jmatprotec.2011.04.016
31. Voliotis A, Bezantakos S, Giamarelou M, Valenti M, Kumar P, Biskos G (2014) Nanoparticle emissions from traditional pottery manufacturing. [Research Support, Non-U S Gov't]. Environ Sci Process Impacts 16(6):1489–1494
32. Jacobs CWF (1954) Opacifying crystalline phases present in zirconium-type glazes. J Am Ceram Soc 37(5):216–220. doi:10.1111/j.1151-2916.1954.tb14026.x
33. Romero M, Rincón JM, Acosta A (2003) Crystallisation of a zirconium-based glaze for ceramic tile coatings. J Eur Ceram Soc 23(10):1629–1635. doi:10.1016/S0955-2219(02)00415-6
34. Lahoz R, de la Fuente GF, Pedra JM, Carda JB (2011) Laser engraving of ceramic tiles. Int J Appl Ceram Technol 8(5):1208–1217. doi:10.1111/j.1744-7402.2010.02566.x
35. Casasola R, Rincón JM, Romero M (2012) Glass–ceramic glazes for ceramic tiles: a review. J Mater Sci 47(2):553–582. doi:10.1007/s10853-011-5981-y
36. Celades I (2013) Caracterización física, química, mineralógica y morfológica del material particulado emitido por focos canalizados de la industria de baldosas y fritas cerámicas. PhD, Universitat Jaume I de Castellón, Castellón
37. NIOSH (2011) Occupational exposure to titanium dioxide, current intelligence bulletin 63. http://www.cdc.gov/niosh/docs/2011-160/pdfs/2011-160.pdf
38. IARC (2010) The International Agency for Research on Cancer. IARC monographs on the evaluation of carcinogenic risks to humans: carbon black, titanium dioxide, and talc, vol 93. World Health Organization, International Agency for Research on Cancer, Lyon http://monographs.iarc.fr/ENG/Monographs/vol93/index.php

39. NIOSH (2007) NIOSH pocket guide to chemical hazards. Department of Health and Human Services, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health. http://www.cdc.gov/niosh/npg
40. IARC (1987) Overall evaluations of carcinogenicity: an updating of IARC Monographs volumes 1 to 42. IARC Monogr Eval Carcinog Risks Hum Suppl 7:1–440
41. NIOSH (1988) NIOSH testimony to the U.S. Department of Labor: statement of the National Institute for Occupational Safety and Health. Presented at the public hearing on OSHA PELS/Crystalline Silica, July 1988. NIOSH Policy Statements, Cincinnati
42. DHHS (1991) Sixth annual report on carcinogens: summary 1991. In: N.U.S.D.o.H.a.H.S. Research Triangle Park, Public Health Service, National Institute of Environmental Health Sciences (ed), pp 357–364
43. ECHA (2015) Information on chemicals. Registered substances http://echa.europa.eu/information-on-chemicals/registered-substances. Accessed 14 Apr 2015
44. ACGIH (2015) Threshold limit values for chemical substances and physical agents and biological exposure indices. In: American Conference of Governmental Industrial Hygienists, http://www.acgih.org. ISBN: 978-1-607260-77-6
45. OSHA (2006) Regulations (Standards – 29 CFR) – Table of Contents, 29 CFR 1910.1000. Z-3. U.S. Department of Labor, Occupational Safety & Health Administration, Washington DC, USA
46. IFA (2009) Technical Information – Nanoparticles at the workplace. http://www.dguv.de/ifa/Fachinfos/Nanopartikel-am-Arbeitsplatz/index-2.jsp
47. Schmatjko KJ, Endres G, Schmidt U, Banz PH (1988) Precision machining of ceramic materials by excimer laser irradiation. In: Proceedings of the SPIE 0957, laser beam surface treating and coating, 119 (October 24, 1988); doi:10.1117/12.947710
48. Toenshoff HK, Gedrat O (1991) Absorption behavior of ceramic materials irradiated with excimer lasers. In: Proceedings of the SPIE 1377, excimer laser materials processing and beam delivery systems, 38 (March 1, 1991). doi:10.1117/12.48071
49. Jervis TR, Nastasi M, Hubbard KM, Hirvonen JP (1993) Excimer laser surface processing of ceramics: process and properties. J Am Ceram Soc 76(2):350–355. doi:10.1111/j.1151-2916.1993.tb03791.x
50. de Francisco I, Lennikov VV, Bea JA, Vegas A, Carda JB, de la Fuente GF (2011) In-situ laser synthesis of rare earth aluminate coatings in the system Ln-Al-O (Ln=Y, Gd). Sol State Sci 13 (9):1813–1819. doi:10.1016/j.solidstatesciences.2011.07.013
51. Estepa C, de la Fuente GF (2006) Continuous Furnace with Coupled Laser for the Surface Treatment of Materials. Patent No. 200600560
52. Bäuerle D (1996) Laser processing and chemistry. Springer-Verlag, Berlin
53. Rubahn H-G (1999) Laser applications in surface science and technology. Wiley, New York
54. Methner M, Hodson L, Geraci C (2010) Nanoparticle Emission Assessment Technique (NEAT) for the identification and measurement of potential inhalation exposure to engineered nanomaterials—part A. J Occup Environ Hyg 7(3):127–132. doi:10.1080/15459620903476355
55. VCI, BAuA, RCI, B, IFA, IUTA, TUD (2011) Tiered approach to an exposure measurement and assessment of nanoscale aerosols released from engineered nanomaterials in workplace operations. https://www.vci.de/vci/downloads-vci/tiered-approach.pdf
56. Asbach C, Kuhlbusch T, Kaminski H, Stahlmecke B, Plitzko S, Götz U, Voetz M, Kiesling HJ, Dahmann D (2012) NanoGEM Standard operation procedures for assessing exposure to nanomaterials, following a tiered approach. Federal Ministry of Education and Research. http://www.nanogem.de/cms/nanogem/upload/Veroeffentlichungen/nanoGEM_SOPs_Tiered_Approach.pdf
57. Fierz M, Houle C, Steigmeier P, Burtscher H (2011) Design, calibration, and field performance of a miniature diffusion size classifier. Aerosol Sci Technol 45(1):1–10. doi:10.1080/02786826.2010.516283

58. Misra C, Singh M, Shen S, Sioutas C, Hall PM, Sioutas C, Hall PM (2002) Development and evaluation of a personal cascade impactor sampler (PCIS). J Aerosol Sci 33:1027–1047
59. Querol X, Alastuey A, Rodríguez S, Plana F, Ruiz CR, Cots N, Massagué G, Puig O (2001) PM10 and PM2.5 source apportionment in the Barcelona Metropolitan Area, Catalonia, Spain. Atmos Environ 35:6407–6419
60. Brouwer D, van Duuren-Stuurman B, Berges M, Jankowska E, Bard D, Mark D (2009) From workplace air measurement results toward estimates of exposure? Development of a strategy to assess exposure to manufactured nano-objects. J Nanopart Res 11(8):1867–1881. doi:10.1007/s11051-009-9772-1
61. ICRP (1994) International commission on radiological protection: human respiratory tract model for radiological protection. ICRP Publication/Elsevier, Tarrytown p 66
62. Kaminski H, Beyer M, Fissan H, Asbach C, Kuhlbusch TAJ (2015) Measurements of nanoscale TiO_2 and Al_2O_3 in industrial workplace environments – methodology and results. Aerosol Air Qual Res 15(1):129–141. doi:10.4209/aaqr.2014.03.0065
63. Fonseca AS, Viana M, Querol X, Moreno N, de Francisco I, Estepa C, de la Fuente GF (2015) Ultrafine and nanoparticle formation and emission mechanisms during laser processing of ceramic materials. J Aerosol Sci 88:48–57
64. Kumar P, Fennell P, Britter R (2008) Effect of wind direction and speed on the dispersion of nucleation and accumulation mode particles in an urban street canyon. Sci Total Environ 402 (1):82–94. doi:10.1016/j.scitotenv.2008.04.032
65. Peters TM, Heitbrink WA, Evans DE, Slavin TJ, Maynard AD (2006) The mapping of fine and ultrafine particle concentrations in an engine machining and assembly facility. Ann Occup Hyg 50(3):249–257
66. Koivisto AJ, Hussein T, Niemelä R, Tuomi T, Hämeri K (2010) Impact of particle emissions of new laser printers on modeled office room. Atmos Environ 44(17):2140–2146. doi:10.1016/j.atmosenv.2010.02.023
67. Dylla H, Hassan M (2012) Characterization of nanoparticles released during construction of photocatalytic pavements using engineered nanoparticles. J Nanopart Res 14(4):1–15. doi:10.1007/s11051-012-0825-5
68. Azarmi F, Kumar P, Mulheron M (2014) The exposure to coarse, fine and ultrafine particle emissions from concrete mixing, drilling and cutting activities. J Hazard Mater 279:268–279. doi:10.1016/j.jhazmat.2014.07.003
69. Jordán MM, Álvarez C, Sanfeliu T (2006) Spherical particles as tracers of atmospheric ceramic industry. Environ Geol 51(3):447–453. doi:10.1007/s00254-006-0339-5
70. Sanfeliu T, Jordán M, Gómez E, Alvarez C, Montero M (2002) Contribution of the atmospheric emissions of Spanish ceramics industries. Environ Geol 41(5):601–607. doi:10.1007/s002540100427
71. Minguillon MC, Monfort E, Querol X, Alastuey A, Celades I, Miro JV (2009) Effect of ceramic industrial particulate emission control on key components of ambient PM10. [Research Support, Non-U S Gov't]. J Environ Manage 90(8):2558–2567
72. Sánchez de la Campa AM, de la Rosa JD, González-Castanedo Y, Fernández-Camacho R, Alastuey A, Querol X, Pio C (2010) High concentrations of heavy metals in PM from ceramic factories of Southern Spain. Atmos Res 96(4):633–644. doi:10.1016/j.atmosres.2010.02.011
73. Querol X, Viana M, Alastuey A, Amato F, Moreno T, Castillo S, Pey J, de la Rosa J, Sánchez de la Campa A, Artíñano B, Salvador P, García Dos Santos S, Fernández-Patier R, Moreno-Grau S, Negral L, Minguillón MC, Monfort E, Gil JI, Inza A, Ortega LA, Santamaría JM, Zabalza J (2007) Source origin of trace elements in PM from regional background, urban and industrial sites of Spain. Atmos Environ 41(34):7219–7231. doi:10.1016/j.atmosenv.2007.05.022
74. Seinfield JH, Pandis SN (2012) Atmospheric chemistry and physics: from air pollution to climate change. Wiley, New Jersey. ISBN: 9781118591369. https://books.google.es/books?id=YH2K9eWsZOcC

75. Viana M, Rivas I, Querol X, Alastuey A, Sunyer J, Álvarez-Pedrerol M, Bouso L, Sioutas C (2014) Indoor/outdoor relationships and mass closure of quasi-ultrafine, accumulation and coarse particles in Barcelona schools. Atmos Chem Phys 14(9):4459–4472. doi:10.5194/acp-14-4459-2014
76. Kuhlbusch TAJ, Quass U, Koch M, Fissan H, Bruckmann P, Pfeffer U (2004) PM10 source apportionment at three urban back ground sites In the western Ruhr-area, Germany. J Aerosol Sci 35(Suppl 1):79–90. doi:10.1016/j.jaerosci.2004.06.027
77. Albuquerque PC, Gomes JF, Bordado JC (2012) Assessment of exposure to airborne ultrafine particles in the urban environment of Lisbon, Portugal. J Air Waste Manag Assoc 62 (4):373–380
78. Gomes J, Bordado J, Albuquerque P (2012) On the assessment of exposure to airborne ultrafine particles in urban environments. J Toxicol Environ Health A 75(22–23):1316–1329
79. Reche C, Viana M, Brines M, Pérez N, Beddows D, Alastuey A, Querol X (2015) Determinants of aerosol lung-deposited surface area variation in an urban environment. Sci Total Environ 517:38–47. doi:10.1016/j.scitotenv.2015.02.049
80. de la Fuente (2013) Laser applications in industry. China University of Geosciences, Wuhan

Quantitative Modelling of Occupational Exposure to Airborne Nanoparticles

Laura MacCalman, Araceli Sánchez-Jiménez, Emmanuel Belut, Romain Guichard, Martie van Tongeren, Lang Tran, and John Cherrie

Abstract It is important to quantify the exposures experienced by workers in order to implement procedures to reduce exposure as well in the short-term but also to evaluate the impact of exposure on health in the long-term. As it stands measurement of engineered nanomaterials (ENM) is not straightforward and so we increasingly look for exposure models and tools to estimate the exposures experienced by workers. Here we describe two such models which are being used to estimate size-resolved concentrations in space and time after emission, while accounting for agglomeration, dispersion, diffusion and deposition. The CFD model describes the space in detail and models how the particles move around the room in three dimensions, while the two-box model simplifies the space to two boxes. Though they differ in their complexity they both aim to evaluate the concentrations in the space and time, the results of which could be used to evaluate worker's exposure to ENM from specific processes.

Keywords Computational fluid dynamic model, Exposure modelling, Nanomaterials, Two-box model

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1 Introduction

The measurement of engineered nanomaterials (ENM) can often prove challenging, due to limitations of the current equipment to track changes in the physico-chemical characteristics of the particles and the few suitable personal monitors that are commercially available. As a result, modelling of exposures is becoming more important in the risk assessment of ENM. Currently within the field of risk assessment of ENM there are a number of qualitative and semi-quantitative control banding tools which aim to estimate the hazard and exposure potential, under certain exposure conditions for specific materials, which when combined provide a risk category (Stoffenmanager Nano, Nanosafer, CB Nanotool). These control banding tools make recommendations on controls that could be put in place to mitigate the exposure potential, thus reducing the risk. While these tools can be very useful to identify potential for exposure and tier 1 risk assessment, they don't provide quantitative estimates of exposure.

Quantitative models have been developed which provide estimates of concentrations in the micro-size range such as those described by Tielemans et al. [1], Marquart et al. [2], Fransman et al. [3] and Cherrie et al. [4] which are used in Stoffenmanager and the Advanced REACH Tool (ART). These models describe the movement of particles from an emission source to a receptor (the worker). They are mechanistic models that have been calibrated with data from exposure measurement surveys. They provide the total inhalable concentration and do not take account of the particle size distribution (PSD). The PSD is however important as the aerodynamic diameter of the particles will determine the likelihood that particles will be deposited in the lower airways. The PSD of the particles may shift during the transfer from the source to the receptor due to deposition and diffusion

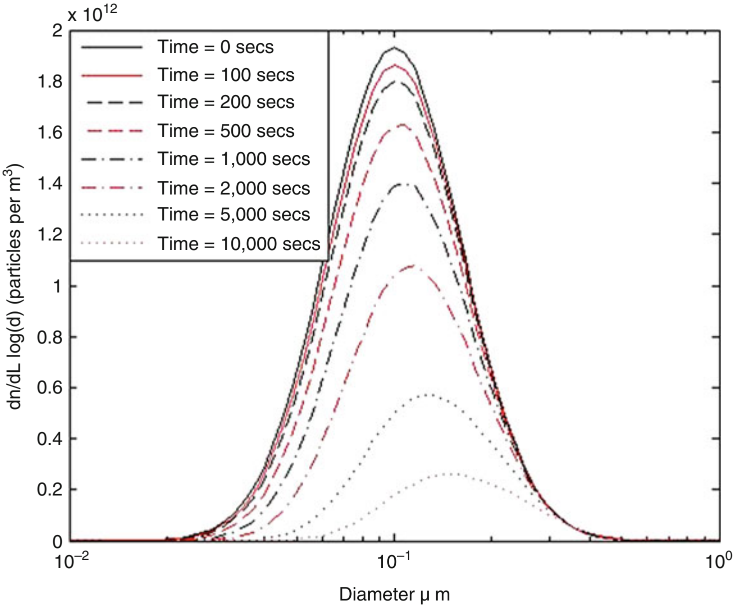

Fig. 1 Shift of the particle size distribution to larger sizes due to the effects of coagulation

losses as well as agglomeration and scavenging (Schneider et al. [5]). Coagulation of particles in the nano-size range can be important when concentrations are sufficiently high ($>$10,000 particles cm^{-3}) (Koivisto et al. [6]), which essentially results in the PSD shifting to larger particles and the peak decreasing (lower number of particles). This is illustrated in Fig. 1, where a single burst of particles with GMD 100 nm, GSD 1.6 and concentration of 10^{12} particles/m^3 was modelled over 10,000 s.

This chapter summarizes two models that could be used to estimate concentrations in the nano-size range; the computational fluid dynamics (CFD) exposure model and the nano-specific two-box (NSTB) exposure model.

2 The CFD Model

The use of models based on Computational Fluid Dynamics (CFD) can provide a more accurate estimate of exposure to airborne nanoparticles in the indoor environment. In this section we introduce and illustrate such a modelling approach. CFD models allow prediction of the 3D flow patterns in ventilated rooms, together with concentration fields of pollutants, by solving the partial differential equations which rule the physics of the time and space evolution of pressure, air velocity fields and particles concentration in well-defined domains such as rooms.

2.1 Assumptions and Modelling of the Fluid Flow

For typical indoor air conditions, the air can be considered as an incompressible fluid undergoing slow turbulent motion. We shall assume here that the mean air velocity and pressure fields are given by any suitable CFD model, so that we can focus on the modelling of nanoparticle transport. A suitable CFD model for indoor air applications should be able to cope with the complexity of geometries encountered in rooms, and with flows where separation, recirculation or buoyancy occur. For ventilation studies, the Reynolds Averaged Navier–Stokes (RANS) approaches are generally used, among which the $k-\varepsilon$ realizable [7] and $k-\varepsilon$ RNG [8] closure models are generally preferred [9, 10]. Any other Eulerian approaches providing an accurate prediction of the three-dimensional airflow of interest (other RANS models or Large Eddy Simulation, for instance) are also compatible with the further described modelling of nanoparticle transport.

It should be emphasized that for indoor air applications and for aerosols in general, the aerosol Péclet number is very large, i.e. aerosol transport is largely dominated by convection. For that reason, an erroneous modelling of the airflow field is the main cause of error while modelling aerosol dispersion by means of CFD. Before attempting to model aerosol transport, it is therefore of primary importance to carefully model the motion of the carrying air.

2.2 Assumptions to Model the Transport of Nanoparticles and Associated Aggregates

The aerosol, composed of nanoparticles or of nanoparticle aggregates, is assumed sufficiently dilute (volume fraction below 10^{-6}) and with a sufficiently low inertia (particle relaxation time lower than the Kolmogorov time scale, in practice for most indoor air application this corresponds to aerosols with an aerodynamic diameter lower than about 10 μm) so that its influence on the carrier flow is negligible. Reactive particles are not presently considered, nor are phase changes. In this framework, a so-called one-way coupling approach is suitable to predict the aerosol motion [11]. This means that the airflow motion can be modelled independently from the aerosol.

As stated previously, we hence assume that the Eulerian mean velocity field in the considered domain is given in each point by a CFD model and so are the mean static pressure and turbulent diffusivity. Non-isothermal airflows can be considered but thermal phenomena affecting aerosols (thermophoresis, etc.) are not taken into account in this chapter. The effect of electric charges is also disregarded despite its influence on particle deposition.

The model intends to treat cases where particle number concentration is high (aerosols of nanoparticles), in which case agglomeration of particles is taken into account. Agglomeration of particles is assumed to be ruled by Brownian motion and turbulence of the carrying airflow only. Each collision of particles is assumed to lead to particle agglomeration, the total mass being conserved in the process. Note that even if this hypothesis of perfect sticking is true for Brownian coagulation [12], it should be considered with caution when both colliding particles are greater than a few hundred nanometres (but in that case the number concentration is generally sufficiently low so that the collision rate is already very small, which makes agglomeration negligible).

Particles are assumed to behave like their equivalent sphere in aerodynamic diameter. The asphericity of particles is considered for agglomeration only. In case of agglomeration, it is assumed that the aerodynamic diameter of particles is related to their collision diameter by means of a known relationship. This relationship can be based on fractal theory or on geometrical considerations based on TEM (Transmission Electronics Microscope) analysis, such as the ratio of mean Fenet diameter over surface equivalent diameter (for a two-dimensional observation).

2.3 Modelling the Transport of Nanoparticles and Aggregates

An Eulerian point of view is considered to model the transport of nanoparticles and their aggregates.

2.3.1 Transport Equation

Considering the low inertia and the volume fraction of particles, their motion can be well described by a "Drift-Flux" approach [10, 13–16]. In this respect, the transport equation for the numerical concentration of particles of size L through space and time reads

$$\frac{\partial n(L)}{\partial t} + \frac{\partial}{\partial x_i}((U_i + V_{s,i}(L))n(L)) = \frac{\partial}{\partial x_i}\left((D_B(L) + D_T)\frac{\partial n(L)}{\partial x_j}\right) + \Pi_c, \qquad (1)$$

where $n(L)$ is the concentration of particles of size L at time t and position x_i, U_i is the ith component of the fluid mean velocity, $V_{s,i}(L)$ is the ith component of gravitational sedimentation for particles of size L, $D_B(L)$ and D_T are, respectively, the Brownian and the turbulent diffusion coefficients and then Π_c is the coagulation source term.

When the fluid acceleration becomes comparable or higher than the gravitational acceleration, in pipe bends for instance, $V_{s,i}(L)$ can be modified to take into account centrifugal (i.e. deviation) effects. Other effects such as turbophoresis or diffusiophoresis can also be included, in which case the model becomes identical to the diffusion-inertia model of Zaichik et al. [17].

To take into account the particle size distribution (PSD) and the effect of coagulation, a sectional method could be considered but this would lead to dividing the PSD into a great number of sections to keep a reasonable accuracy. Incidentally, a great number (in practice several hundred) of coupled transport equations would have to be solved simultaneously, which would make the computational cost too high. A more efficient method consists of rewriting transport equation (1) in a quadrature method of moments (QMOM) framework. With this technique, only the global properties of the PSD, called the moments, are tracked. Moments are defined by

$$M_k = \int_0^\infty n(L) L^k dL, \tag{2}$$

where M_k is the kth moment of the particle size distribution at time t and position x_i. However, definition 2 applied to the transport equation leads to integro-differential equations which cannot be analytically solved in the general case. To overcome this difficulty, a quadrature approximation of the integrals is adopted [18–22]. Keeping a low computational cost is possible since Marchisio et al. [23] showed that the first six moments are sufficient to correctly describe most particle size distribution, i.e. only six transport equations need to be solved to model the aerosol dispersion. Moreover, some assumptions can be made when considering low-inertia particles in a ventilated room. The turbulent diffusivity is much larger than the Brownian diffusivity, except in the near-wall region where the Brownian diffusivity affects the deposition. If the concentration boundary layer is not solved, the "Drift Flux" transport equation of the moments then takes the following form:

$$\frac{\partial M_k}{\partial t} + U_i \frac{\partial M_k}{\partial x_i} + \Phi_{s,k} = \frac{\partial}{\partial x_i}\left(D_T \frac{\partial M_k}{\partial x_j}\right) + \Pi_{c,k}, \tag{3}$$

where $\Phi_{s,k}$ is the sedimentation flux of moment M_k and $\Pi_{c,k}$ is the coagulation source term of moment M_k. These terms are detailed in the following subsections, together with the boundary condition used to treat the deposition. The isotropic turbulent diffusion coefficient D_T is given by

$$D_T = \frac{\nu_T}{Sc_T}, \tag{4}$$

where Sc_T is the turbulent Schmidt number that is commonly assumed close to unity (here it is equal to one) and ν_T is the fluid turbulent viscosity computed by the CFD solver. In $k - \varepsilon$ turbulence models, $\nu_T = C_\mu k^2/\varepsilon$, where k is the turbulent kinetic energy and ε is the turbulent dissipation rate. According to the chosen closure turbulence model, generally "RNG" or "Realizable" for simulating airflows in ventilated rooms, parameter C_μ takes different values [7, 8]. Equation (3) can be implemented in any CFD solver as a passive scalar transport equation including a source term. The interested reader about the detailed implementation of the transport equation (3) into a commercial CFD code will refer to Guichard et al. [24, 25].

2.3.2 Coagulation Source Term

The temporal change of the moments due to the coagulation phenomenon is given by the following population balance equation (5):

$$\Pi_{c,k} = \int_0^\infty \int_0^\infty \beta\left(L, L'\right)\left(\frac{1}{2}\left(L^3 + L'^3\right)^{k/3} - L^k\right) n(L) n\left(L'\right) dL dL', \tag{5}$$

where $\beta(L, L')$ is the coagulation kernel between particles of size L and particles of size L'.

The coagulation kernel, $\beta(L, L')$, represents the volume integral of the number of coagulation events per unit of time between two homogeneous populations of particles of typical size L and L': this is usually expressed in $\mathrm{m^3 s^{-1}}$. Particle coagulation can be influenced by fluid turbulence effects, thermophoresis (due to temperature gradients), turbophoresis (due to gradients of turbulence levels), gravity effects, etc. However, for nanoparticles in a homogeneous fluid phase, Brownian motion and turbulence are the main phenomena which enhance coagulation [26].

The Brownian and turbulent coagulation kernel described in Guichard et al. [25] is used. It corresponds to the kernel of Zaichik and Solov'ev [27] which has been adapted to take into account the morphology of aggregates. Zaichik and Solov'ev [27] proposed a statistical model to determine the kernel of coagulation of small aerosol particles under both Brownian motion and homogeneous isotropic turbulence. They compared it to direct numerical simulation results with a relative error of about 4% for the turbulence part. The final form of the kernel, which we shall call the statistical coagulation kernel, is expressed as follows:

$$\beta\left(L, L'\right) = \frac{\sqrt{\beta_B^{\mathrm{col}^2} + \beta_T^{\mathrm{col}^2}}}{1 + \frac{\sqrt{\beta_B^{\mathrm{col}^2} + \beta_\mathrm{T}^{\mathrm{col}^2}}}{\beta_B^{\mathrm{coag}}}\left(1 - \pi\frac{\chi}{2} + \chi \tan^{-1}\chi\right)}, \tag{6}$$

where β_B^{col} is the Brownian collision kernel for the free-molecular mode, $\beta_{\mathrm{B0}}^{\mathrm{coag}}$ is the Brownian coagulation kernel for the continuum mode, β_T^{col} is the turbulent collision kernel and χ is a parameter characterizing the relative dominance of the turbulent versus Brownian mechanism of coagulation. This parameter is defined as

$$\chi = \sqrt{\frac{0.15}{\tau_k D_{B_{LL'}}}\sigma}, \tag{7}$$

where $\sigma = \left(L_f + L_f'\right)/2$ is the effective collision radius, the distance at which two particles of typical size L and L' make contact. To evaluate this collision radius, the volume diameter L, used as internal coordinate for coagulation assuming volume conservation, must be distinguished from the collision diameter L_f which defines the geometrical sphere of influence of aggregates. For spherical particles, $L_f = L$, but for other shapes of particle a relationship between L_f and L must be provided. For instance, when considering fractal-like aggregates, composed of monodispersed primary particles called monomers, the collision diameter corresponds to the geometrical diameter, which gives

$$L_f = L_m \left(C \frac{L}{L_m} \right)^{3/D_f}, \tag{8}$$

where L_m is the monomer size, D_f the asymptotic mean fractal dimension and C a coefficient called structure factor. Vanni [28] showed that factor C can be approximated by $C = 0.414 D_f - 0.211$ for $D_f \in [1.5, 2.75]$.

In Eq. (7), $D_{B_{LL'}}$ is the coefficient of relative Brownian diffusion:

$$D_{B_{LL'}} = k_B T \tau_{p_{LL'}} / m, \tag{9}$$

In this coefficient, k_B is the Boltzmann constant, T is the temperature, $\tau_{p_{LL'}}$ expresses the global particle time relaxation given by $\tau_{p_{LL'}} = \left(\tau_{p_L} m_{L'} + \tau_{p_{L'}} m_L \right) / \left(m_L + m_{L'} \right)$ and m is the effective mass of particles expressed as $m = m_L m_{L'} / (m_L + m_{L'})$. The mass of a particle of equivalent spherical diameter L is provided by $m_L = \rho_p \pi L^3 / 6$ and its time relaxation is given by $\tau_{p_L} = \rho_p L^2 Cu(L) / (18\mu)$, where ρ_p is the particle density, μ_f is the dynamic viscosity of the carrier gas and $Cu(L)$ is the Cunningham correction factor that is significant for a nano-sized aerosol. This factor is given by a correlation such as

$$Cu(L) = 1 + (2\lambda_{\text{air}}/L)[1.2 + 0.41 \exp(-0.88(L/(2\lambda_{\text{air}})))]. \tag{10}$$

where λ_{air} is the mean free path of the carrier gas (typically equal to 66 nm for the ambient air at 20°C). The turbulent collision kernel is given by Saffman and Turner [29] as

$$\beta_T^{\text{col}} = \sqrt{\frac{8\pi}{15}} \frac{\sigma^3}{\tau_k}. \tag{11}$$

The continuum Brownian coagulation kernel established by Smoluchowski [30] is defined by

$$\beta_{B0}^{\text{coag}} = 4\pi\sigma D_B , \tag{12}$$

which is better known under the following form expressed as a function of particle sizes L and L':

$$\beta_{B0}^{\text{coag}} = \frac{2k_B T}{3\mu}(L+L')\left(\frac{Cu(L)}{L} + \frac{Cu(L')}{L'}\right). \tag{13}$$

The free-molecular Brownian collision kernel is derived from kinetic theory of gas as

$$\beta_B^{\text{col}} = \sqrt{\frac{8\pi k_B T}{m}}\sigma^2. \tag{14}$$

It should be noted that coagulation kernel 6 is highly dependent on particle sizes L and L' through the collision radius σ. Thus, for large particles, parameter χ tends to ∞ and the Brownian motion can be neglected, so kernel 6 is reduced to the turbulent collision kernel 9. For small particles, parameter χ tends to 0 and the turbulent effects can be neglected, leading to the Brownian coagulation kernel for the entire size range that is expressed by

$$\beta_B^{\text{coag}} = \frac{\beta_{B0}^{\text{coag}}\beta_B^{\text{col}}}{\beta_{B0}^{\text{coag}} + \beta_B^{\text{col}}}, \tag{15}$$

which is actually a combination of the free-molecular mode and the continuum mode. It can be observed that this kernel is very close to the one developed by Fuchs (Eq. (27), used in the two-box model) but it is also less computationally costing. In most published works, coagulation kernels obtained from different physical phenomena are just added together under the assumption that these phenomena are not related, which has not yet been firmly established. It can be shown that adding Brownian and turbulent kernels is incorrect for a range of particle sizes from 100 nm to 8 μm, which corresponds to nanoparticle aggregates.

In practice, Eq. (5) can be solved in a DAE-QMOM framework by using the "Dassl" solver of Petzold [31].

2.3.3 Sedimentation Flux

The sedimentation flux of moment M_k is computed from the gravitational sedimentation velocity as

$$\Phi_{s,k} = \frac{\partial}{\partial x_i}\left(g_i \int_0^\infty \tau_p(L) n(L) L^k dL\right), \tag{16}$$

where g_i is the gravitational acceleration in the spatial direction i and $\tau_p(L)$ is the relaxation time of particles of size L. For the size range of interest, the particle relaxation time is defined by

$$\tau_p(L) = \frac{\rho_p L^2 \mathrm{Cu}(L)}{18\mu_f}. \tag{17}$$

where ρ_p is the particle density, μ_f is the fluid dynamic viscosity and $\mathrm{Cu}(L)$ is still the Cunningham coefficient. The sedimentation flux $\Phi_{s,k}$ is finally added to the pure convection flux in the CFD solver.

2.3.4 Boundary Condition for the Deposition

Since the concentration boundary layer at walls cannot be solved by the model, given that Brownian diffusivity is disregarded in the moments transport equation, the deposition has to be modelled by means of a wall function approach. The flux of particles towards the wall is thus computed following the work of Nérisson et al. [32] who proposed the so-called Dynamic Boundary Layer model. This model provides a treatment for deposition which is directly suitable for implementation in a CFD code. It has no lower limit in terms of particle diameters and may be adapted to any surface orientation and any deposition regime. To compute the theoretical flux of moments towards the wall, the concentration profile in the boundary layer is integrated, leading to the following expression of the deposition flux:

$$J_{d,k}(L) = \int_0^\infty V_d(L) n_b(L) L^k dL, \tag{18}$$

where $n_b(L)$ is the bulk concentration nearby the wall and $V_d(L)$ is the particle deposition velocity, given by

$$V_d(L) = \frac{\mathbf{g}^+(L) \cdot \mathbf{n}\, u*}{1 - \exp\left(\mathbf{g}^+(L) \cdot \mathbf{n}\, I_p(L)\right)}, \tag{19}$$

for any surface orientation. It should be noted that the limit for a vertical wall becomes

$$V_d(L) = \frac{u*}{I_p(L)}. \tag{20}$$

In Eqs. (19) and (20), $u*$ is the fluid-wall friction velocity, $\mathbf{g}^+(L) = \mathbf{g}\tau_p(L)/u*$ is the dimensionless gravitational acceleration vector, $\mathbf{n}$ is the unitary normal vector to the wall (pointing towards the fluid) and $I_p(L)$ is a function defined by

$$I_p(L) = \frac{Sc_T}{\kappa}\ln(y^+) + \left(\frac{\tau_p^{+2}(L)}{1700} + \frac{Sc_B(L)^{-2/3}}{13.7}\right)^{-1}, \tag{21}$$

where κ is the Von Kàrmàn constant equal to 0.41, $\tau_p^+(L)$ is the dimensionless particle relaxation time defined by $\tau_p^+(L) = \tau_p(L)u^{*2}/\nu_f$, where ν_f is the fluid kinematic viscosity. In Eq. (21), $Sc_B(L)$ represents the Brownian Schmidt number, given by

$$Sc_B(L) = \frac{\nu_f}{D_B(L)}, \tag{22}$$

where $D_B(L)$ is the Brownian diffusion coefficient defined as

$$D_B(L) = \frac{k_B T Cu(L)}{3\pi\mu_f L}, \tag{23}$$

where k_B is the Boltzmann constant equal to 1.38×10^{-23} m^2 kg s^{-2} K^{-1} and T is the temperature.

In practice, the bulk concentration $n_b(L)$ that appears in Eq. (18) is chosen in the first near-wall cell. The size of this cell is specified as its centre follows the constraint $y^+ > 30$, where y^+ is the dimensionless wall distance, according to the practical recommendation of Nérisson et al. [32] which proposed the "Dynamic Boundary Layer" deposition model for application in a CFD framework.

The complete model described above was evaluated by comparison with test-cases from the literature [33], and with a dedicated experiment.

2.4 Summary of the Model Parameters

Table 1 outlines the model parameters, the majority of which are dependent on the experimental conditions or the environment of the workplace.

2.5 Using the CFD Model of Nanoaerosol Transport for Workplace Exposure

We previously described the transport equations which model the evolution of the moments of the particle size distribution (PSD) in rooms. Given that only the first 6 moments of the PSD are required to correctly represent it, only six transport equations need to be solved to model workplace exposure. Associated to this set of transport equations, boundary conditions for the deposition of particles at walls

Table 1 Summary of parameters used in the model

Abbreviation	Full name	Type/unit	Value
Ω	Approximate geometrical description of the domain of interest	Computational grid (cells, nodes)	Case dependent
∂Ω	Description of variables at domain boundaries	Values (velocity vectors, pressure, turbulence parameters, aerosol PSD and concentration)	Case dependent
∂M_k	*k*th moment of the particles PSD at boundaries ∂Ω and sources	Particle m^{k-2}	Computable from $n(L)$, the measured particle size distributions at sources and boundaries, following $M_k = \int_0^\infty n(L)L^k dL$
U_i	Mean velocity vectors field in **Ω**	m s^{-1}	Solved by CFD using above parameters
k	Turbulent kinetic energy field in **Ω**	m^2 s^{-2}	Solved by CFD using above parameters
ε	Dissipation rate of k in **Ω**	m^2 s^{-3}	Solved by CFD using above parameters
P	Mean pressure field in **Ω**	Pa	Solved by CFD using above parameters
τ_k	Mean field of Kolmogorov's time scale in **Ω**	s	$\sqrt{{}^{\nu_f}/_{\varepsilon}}$
Cμ	$k-\varepsilon$ model constant	Dimensionless	0.09
$L_f(L)$	Capture diameter of a particle of volumetric diameter *L*	m	Fractals: $L_f = L_m\left(C\frac{L}{L_m}\right)^{3/D_f}$ L_m: monomer size D_f: asymptotic mean fractal dimension C: structure factor. $C = 0.414$ $D_f - 0.211$ for $D_f \in [1.5\ ,\ 2.75]$ (Vanni [26])
T	Mean pressure field in **Ω**	K	Solved by CFD or constant
ρ_f	Air density	kg m^{-3}	1.225 kg m^{-3} at 1,013 hPa, 15°C
ρ_p	Particles elemental density	kg m^{-3}	
μ_f	Air molecular viscosity	Pa s	1.8×10^{-5} Pa s at 1,013 hPa, 15°C
υ_f	Air kinematic viscosity	m^2 s^{-1}	$\nu_f = {}^{\mu_f}/_{\rho_f}$

(continued)

Table 1 (continued)

Abbreviation	Full name	Type/unit	Value
λ_{air}	Mean free path of the air	m	$\lambda_{air} = \lambda_\circ \times \left(\frac{T}{T_\circ}\right)\left(\frac{P}{P_\circ}\right)\left(\frac{1+S/T_\circ}{1+S/T}\right)$ λo = reference free path (λ_{air} 0.0674×10^{-6} m) at T_0 and P_0 T_0 = reference temperature 273.15 K T = temperature (293.15 K) P_0 = reference pressure (1,013 hPa) S = Sutherland constant (110.4 K, at 293.15 K and 1,013 hPa, as discussed in Allen and Raabe [36])
g_i	Gravitational acceleration vector	m s^{-2}	9.81 m s^{-2}
k_B	Boltzmann constant	m^2 kg s^{-2} K^{-1}	1.38×10^{-23} m^2 kg s^{-2} k^{-1}
κ	Von Kàrmàn constant	Dimensionless	0.41
Sc_T	Particles turbulent Schmidt number	Dimensionless	1

were given. The coagulation source term, which allows computing the PSD change due to aggregation/coagulation of particles, was also presented. All these elements can be integrated into a general purpose CFD software and coupled with airflow modelling. This section illustrates an application of the method in a workplace.

2.5.1 Application Case

We consider the case of a rectangular room with dimensions 6.5 × 4.7 × 2.6 m (80 m^3) such as depicted on Fig. 2. This room could be a lab, for instance. It is ventilated with fresh air at an air exchange rate of 10 volumes per hour by two perfectly equilibrated inlets blowing sideways along the roof, such as depicted in the figure (arrows). The air is exhausted through a unique omnidirectional outlet. A nanoparticle source is located in a corner, at 1.2 m for the walls and 1 m above the ground. This source emits continuously an aerosol of nanoparticles (it could be a leak from a reactor, for instance) at a flow rate of 10 l min^{-1}, at a particle number concentration of 6.3×10^6 cm^{-3}. The corresponding particle size distribution presents a geometric mean diameter of 61 nm and a geometric standard deviation of 1.72. The source forms a round jet towards the roof with an initial velocity of 0.6 m s^{-1}. We intend to model the steady-state concentration field of nanoparticles in this room.

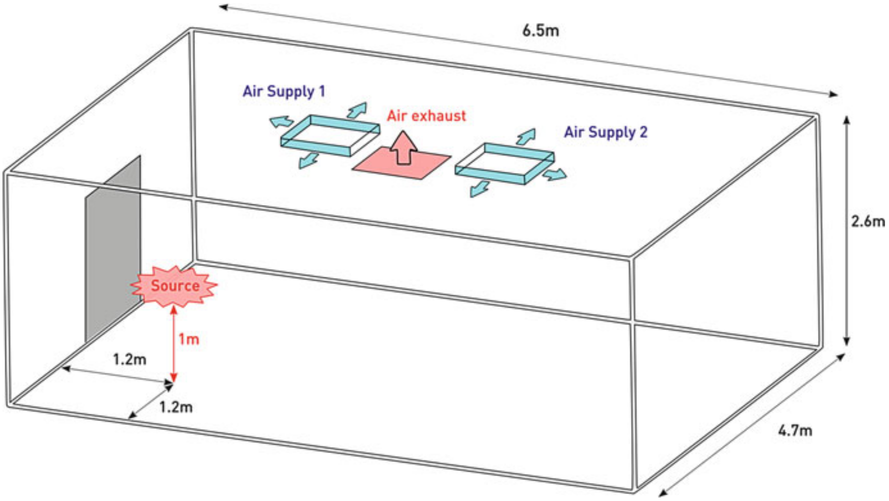

Fig. 2 Application case: a ventilated 80 m^3 room where a nanoparticle source is present

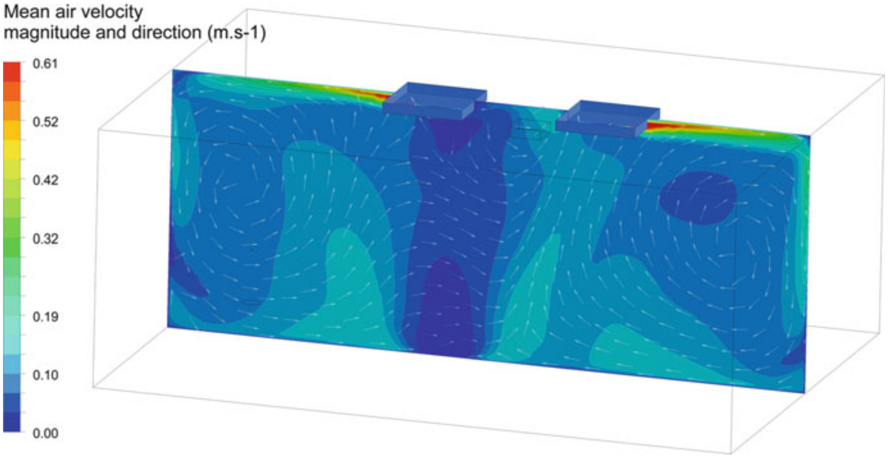

Fig. 3 Airflow mean velocity and direction predicted by CFD in the middle plane

2.5.2 Airflow in the Room

The steady-state airflow in the room is modelled by means of CFD, using a k−ε realizable turbulence model with standard wall functions. The mean velocity field in the room predicted by the CFD model is depicted in Figs. 3 and 4, for two vertical planes situated as shown. The ventilation appears to provide good mixing, though the room appears divided into two main circulation zones, each being dominated by one of the two inlets.

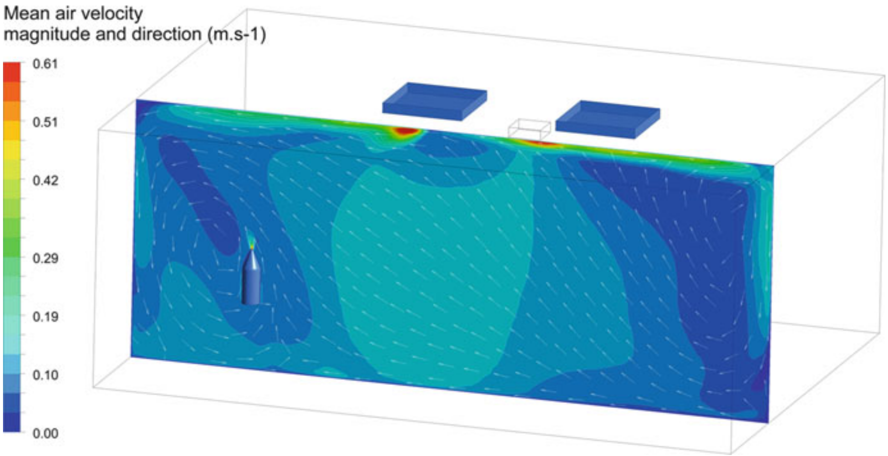

Fig. 4 Airflow mean velocity and direction predicted by CFD in the nanoparticles source plane

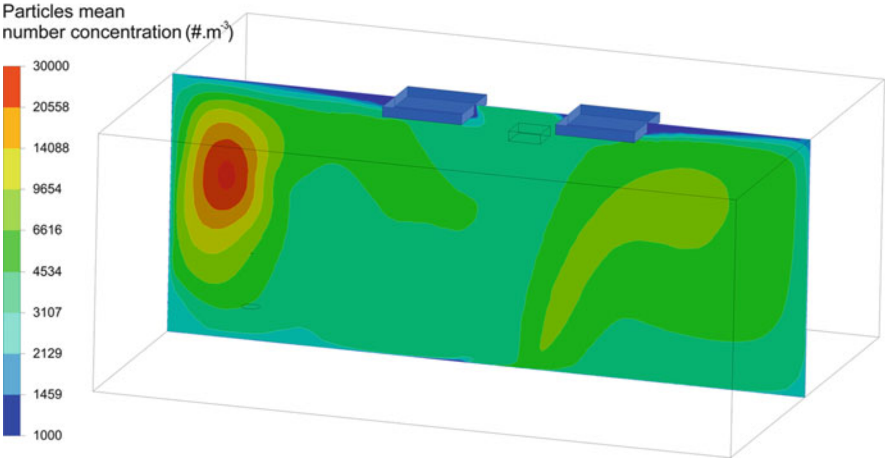

Fig. 5 Aerosol mean number concentration (# m^{-3}) computed in the middle plane

2.5.3 Nanoparticles Number Concentration in the Room

The mean airflow computed in the room can be used together with the nanoparticle transport model to calculate the aerosol mean number concentration fields shown in Figs. 5 and 6.

As could be deduced from the source position and from the flow pattern, the left side of the room appears more polluted, even if the aerosol is globally well mixed in the room, with an average number concentration of a few ten thousand. The left recirculation zone tends to maintain a higher pollutant concentration in the leftmost area. This kind of computation shows how the model can be used to predict the level of exposure to which an operator would be exposed.

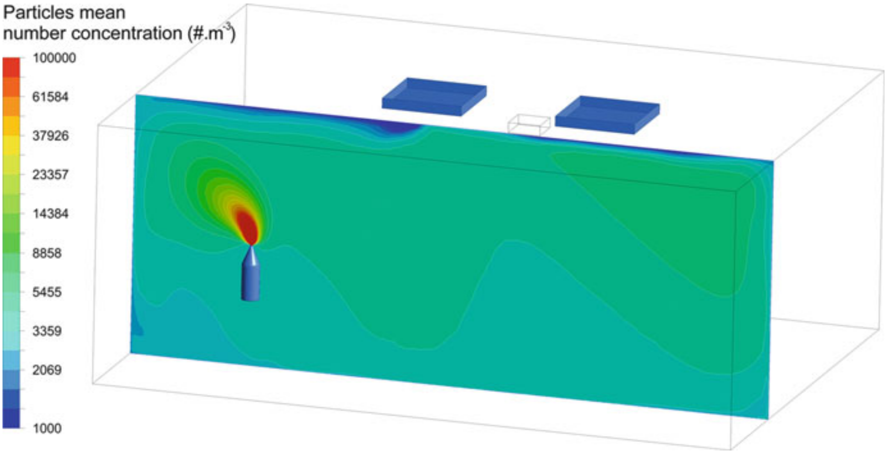

Fig. 6 Aerosol mean number concentration (# m^{-3}) computed in the nanoparticle source plane

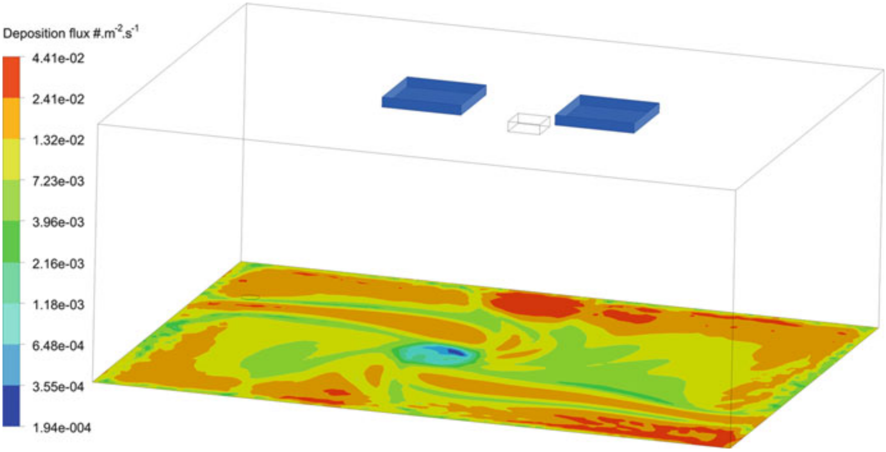

Fig. 7 Particles mean deposition flux computed on the floor of the cabin

2.5.4 Predicting Nanoparticles Deposition on Surfaces

Incidentally, the nanoparticles CFD model also allows computing the deposition flux of particles on surfaces, which provides interesting applications for surface contamination studies. Figure 7 thus shows the computed deposition flux of nanoparticles on the floor of the studied cabin. This kind of prediction allows locating where surfaces will be most polluted, which can be used to help sampling strategies or for cleaning purposes. It also makes it possible to design the ventilation system so as to minimize surface contamination, for instance.

The CFD model allows for a detailed description of the particle movement over time and space which can be used to evaluate worker's occupational exposure as they move about their workspace. The implementation of such a model requires a very high degree of expertise, first in setting up the inputs required by the CFD model, then in running the CFD model. This level of expertise is not typically found in those who want to obtain estimates of the concentrations worker's are exposed to over a work shift. In addition, workplaces are often very complex dynamic environments, which makes it extremely complicated to model using a CFD approach. For this purpose the model needs to be simplified somewhat, and the following section describes a model which is based on the same principles of aerosol physics as the CFD model but does not consider space in such detail.

3 Two-Box Nano-Specific Exposure Model

The model is based on the Near-Field (NF) Far-Field (FF) source-receptor model developed by Cherrie [4] and the algorithms developed by Maynard and Zimmer [34] for estimating the time evolution PSD of nanoparticles. In a two-box (or -source-receptor) model the room is typically split into two boxes (Fig. 8), one is placed either around the worker or source, while the other is the remainder of the room. These are usually termed as Near-Field (NF) and Far-Field (FF). Some argue that the NF should be centred around the worker (i.e. a virtual 2 m side cube centred on the worker) as the ultimate aim is to estimate worker exposure [4], while others have argued that the NF should be the region around the source. We will base our definitions on the conceptual model of nano-exposure described in Schneider et al. [5] (Fig. 9) and use the term the local control influence zone (LCIZ) as the box around the source as this is a region that represents the zone of influence for a given local control system, while we define the worker-NF as the volume centred around the worker (Fig. 9). Since the worker moves around the room, the concentration in the worker-NF can be estimated from the concentrations in the LCIZ and FF and the time he/she spends in each zone. In the nano-specific model, other size-dependent factors are taken into account such as coagulation and losses through

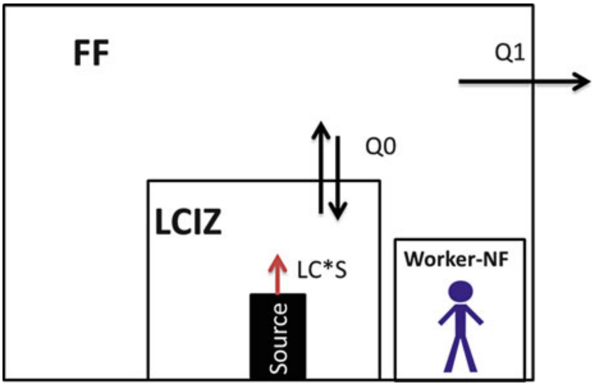

Fig. 8 Illustration of the two-box model; local control influence zone (LCIZ) and far-field (FF). The picture shows the local control adjusted emission (LC × S), the air exchange between the two boxes (Q0) and the ventilation (Q1)

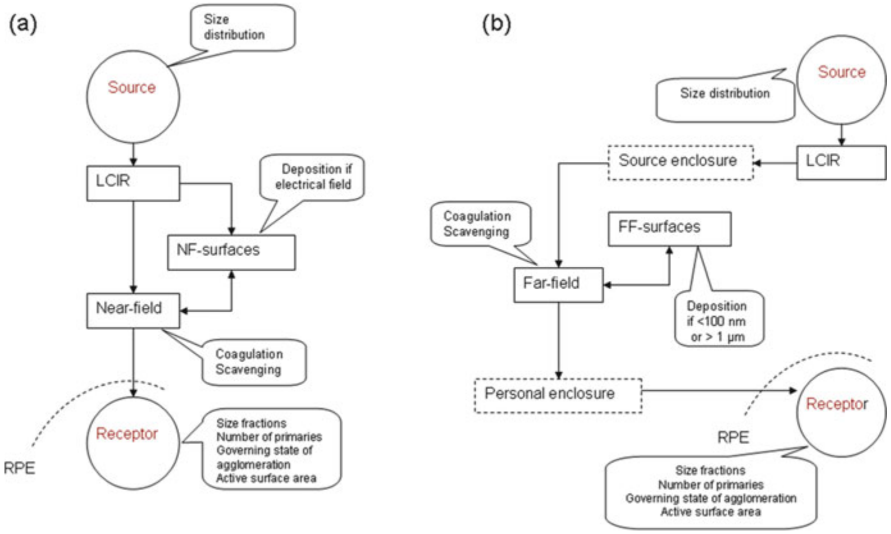

Fig. 9 Conceptual model for assessment of inhalation exposure to engineered nanomaterials presented by Schneider et al. [5]. (**a**) near-field (NF) source and (**b**) far-field (FF) source. Reprinted by permission from Macmillan Publishers Ltd: [JESEE] [5]

gravitational settling (particles settling to the floor), diffusion (particles settling on walls and surfaces) and dilution (effect of ventilation).

In order to estimate the particle size distribution over time it is split into a number of bins of particles of size: $L_1, \ldots, L_j, \ldots, L_N$. The number of particles in each bin is then estimated over time, this is done separately for both LCIZ and FF.

The concentration in either zone is then a function of agglomeration, diffusion, dispersion, dilution and emission, with each particle size bin in each zone (LCIZ or FF) being described using the following equations:

$$\frac{dn(L_j)_{\mathrm{LCIZ}}}{dt} = \mathrm{LC} \times S_{\mathrm{LCIZ}} - n(L_j)_{\mathrm{LCIZ}}\frac{Q_{\mathrm{LCIZ}}}{V_{\mathrm{LCIZ}}} + n(L_j)_{\mathrm{FF}}\frac{Q_{\mathrm{LCIZ}}}{V_{\mathrm{LCIZ}}} + \eta_{\mathrm{LCIZ}}, \quad (24)$$

$$\begin{aligned}\frac{dn(L_j)_{\mathrm{FF}}}{dt} &= \mathrm{LC} \times S_{\mathrm{FF}} \\ &\quad + n(L_j)_{\mathrm{LCIZ}}\frac{Q_{\mathrm{LCIZ}}}{V_{\mathrm{FF}}} - n(L_j)_{\mathrm{FF}}\frac{Q_{\mathrm{LCIZ}}}{V_{\mathrm{FF}}} - n(L_j)_{\mathrm{FF}}\frac{Q_{\mathrm{FF}}}{V_{\mathrm{FF}}} + \eta_{\mathrm{FF}} \quad (25)\end{aligned}$$

where LCIZ is a virtual zone that represents the area of influence of any exposure control around the source, Q_{LCIZ} is the volume airflow between the LCIZ and FF (m^3/s); Q_{FF} represents the ventilation (m^3/s); S_{LCIZ} and S_{FF} represent the mass emission rate into the LCIZ and FF, respectively, in particles/s; LC represents the local control adjustment factor and η represents the size-specific factors (coagulation, diffusion and dispersion)

$$\eta = \frac{dn(L_j)}{dt} = \frac{1}{2}\int_{\mathrm{o}}^{L_j} n(L_i)\ \beta(L_i, L_j - L_i)\ n(L_j - L_i)\ dL_i \\ -n(L_j)\int_{\mathrm{o}}^{L_N} \beta(L_j, L_i)\ n(L_i)\ dL_i\ - \frac{n(L_j)v_{ts}}{h} - \frac{A\ \ n(L_i)\ \ D}{V\ \ \delta_{\mathrm{diff}}}. \tag{26}$$

3.1 Coagulation

The coagulation of particles is estimated using the continuous coagulation equation described by Smoluchowski [30] [Eq. (27)]. In the continuum region the distribution of particles around the fixed absorbing particle can be described by a continuum diffusion equation where $n(L, t)$ is the number concentration of particles of size L_i at time t. The first term of the equation represents the formation of particles of size L_i by the coagulation of smaller particles of sizes L_j–L_i. The factor ½ is introduced because collisions are counted twice in the integral. The second factor of the equation represents losses through the coagulation of particles of size L_j with all other particles.

$$\frac{dn(L_j)}{dt} = \frac{1}{2}\int_{\mathrm{o}}^{L_j} n(L_i)\ \beta(L_i, L_j - L_i)\ n(L_j - L_i)\ dL_i \\ -n(L_j)\int_{\mathrm{o}}^{L_N} \beta(L_j, L_i)\ n(L_i)\ dL_i, \tag{27}$$

The equation assumes particles of any size can coagulate to form aggregates of N number of primary particles of size j. Collisions of three particles are ignored for now as they are only important for high concentrations. Considering only Brownian coagulation, the coagulation coefficient of particles in bin j with those in bin i reduces to

$$\beta = f_{ij}\beta_{\mathrm{B0}}^{\mathrm{coag}}, \tag{28}$$

where $\beta_{\mathrm{B0}}^{\mathrm{coag}}$ is defined in Eq. (12) (with $L = L_i$ and $L' = L_j$) and f_{ij} is the Fuchs correction factor [Eq. (29)]. It can be shown that expression (28) is very close to β_B^{coag} defined in Eq. (15) for pure Brownian coagulation and used in the CFD model (see Sect. 2.3.2). The coagulation coefficient for particles in the micro range has to be adjusted as in the nano-range not all the collisions will be successful, i.e. the coagulation rate does not equal the collision rate. We have used the Fuchs correction that assumes NPs move in a transition regime (between free-molecular path and continuum regime) (Seinfeld and Pandis [35]).

The Fuchs correction factor is determined via

$$f_{ij} = \left(\frac{L_i + L_j}{L_i + L_j + 2\delta_{i,j}} + \frac{8D_{B_{ij}}}{v_{i,j}\left(L_i + L_j\right)} \right)^{-1}, \tag{29}$$

$$\delta_i = \left(\frac{1}{3L_i \lambda_{p_i}} \left[\left(L_i + \lambda_{p_i}\right)^3 - \left(L_i^2 + \lambda_{p_i}^{\,2}\right)^{(3/2)} \right] - L_i \right); \delta_{i,j} = \sqrt{\delta_i^2 + \delta_j^2}, \tag{30}$$

where $D_{B_{ij}}$ is defined by Eq. (9) (with $L = L_i$ and $L' = L_j$) and where the particle mean free path (λ_{pi}) is

$$\lambda_{pi} = \frac{8D_B(L_i)}{\pi v_i} \tag{31}$$

In this equation, $D_B(L_i)$ is defined in Eq. (23). The thermal velocity is

$$v_i = \sqrt{\frac{8\,k_b T}{\pi m_i}} \qquad v_{i,j} = \sqrt{v_i^2 + v_j^2}, \tag{32}$$

where assuming spherical particles the mass m_i of the agglomerate can be expressed as

$$m_i = N \frac{\pi \rho_p {L_m}^3}{6}, \tag{33}$$

where ρ_p is the agglomerate elemental density, N is the number of particles in the agglomerate and L_m is the diameter of primary particles (monomers).

The mass of the agglomerate is the sum of the mass of all primary particles in the agglomerate:

$$N \frac{\pi \rho_p {L_m}^3}{6} = \frac{\pi \rho_p {L_i}^3}{6}. \tag{34}$$

Therefore, the number of particles in the agglomerate is

$$N = \left(\frac{L_i}{L_m} \right)^3, \tag{35}$$

where $L_i =$ the diameter of the agglomerate (mid-point of the bin). For each bin the number of particles in the agglomerate does not change over time (as the two components, L_m and L_i do not change).

3.2 *Gravitational Settling and Diffusion Losses*

The rate of particle loss through gravitational settling assuming continuous mixing is estimated as described in Eq. (36) (Maynard and Zimmer [34]).

$$\frac{dn(L_j)}{dt} = -\frac{n(L_j)v_{ts}}{h}, \tag{36}$$

where h is the distance from the source to the deposition surface (m) and v_{ts} is the particle settling velocity (m s^{-1}):

$$v_{ts} = \frac{\rho_p L_i^2 g Cu(L)}{18\mu_f}, \tag{37}$$

ρ_p is the particle density (1,000 kg m^{-3}), $\mu_f =$ viscosity of air (1.807×10^{-5} Pa s at 293.15 K and 1,013 hPa) and g denotes gravity (9.81 m s^{-2}).

The rate of particle loss through diffusion is estimated as

$$\frac{dn(L_j)}{dt} = -\frac{A\, n(L_j)\, D_b(L_j)}{V\,\delta_{\text{diff}}}, \tag{38}$$

where V is the room volume (m^3), A is the total surface area available for deposition (e.g. walls, ceilings, floors) (m^2) and $\delta_{\text{diff}} =$ diffusion boundary layer depth at the surfaces, which is a function of particle diameter and air movement at the boundary:

$$\delta_{\text{diff}} = c D_b(L), \tag{39}$$

where c is an empirically determined constant that is dependent on the geometry and conditions being modelled and α is expected to lie between 1/2 and 1/3 (Maynard and Zimmer [34]). In Maynard and Zimmer's study, the values that better adjusted to the experimental data were $c = 0.050 \pm 0.005$ m$^{1/3}$ s$^{1/3}$ and $\alpha = 1/2$. We also used these values.

3.3 Mass Conservation

The approach used to resolve the differential equation for the coagulation rate does not conserve the mass (i.e. the mass of the agglomerate m_k formed by particles of mass m_i and m_j does not equal $m_i + m_j$). To conserve the mass the differential equation is multiplied by the following expression:

$$\frac{m_i + m_j}{m_k}. \tag{40}$$

3.4 Summary of the Model Parameters

Table 2 outlines the model parameters, the majority of which are dependent on the experimental conditions or the environment of the workplace.

Table 2 Summary of parameters used in the model

Abbreviation	Full name		Value
A	Surface deposition area	m	
D	Stokes's diffusion coefficient	$m^2\ s^{-1}$	
L, L_i, L_j	Particle diameters assumed to be the mid-point of the bin	m	
dm	Mobility diameter	m	
h	Distance from the source to the deposition surface	m	
k_B	Boltzmann's constant	$m^2\ kg\ s^{-2}\ K^{-1}$	1.381×10^{-23} N m K^{-1} at $T = 293.15$ K and $P = 101.3$ Pa
h	Characteristic height of the model system	m	
P	Pressure	Pa	1,013 hPa
S	Particle source	Particles $m^{-3}\ s^{-1}$	
V	Room volume	m^3	
L_m	Diameter of the primary particle	m	
T	Temperature	K	293.15 K
α	Empirically determined constant	Unitless	
δ_{diff}	Diffusion boundary layer depth at the surface	m	
μ_f	Viscosity of the air	Pa s	$\mu_f = \mu_{f_0} + \left(\frac{T_r+S}{T+S}\right)\left(\frac{T}{T_0}\right)^{3/2}$ μ_{f_0}; = reference viscosity at T_r (1.708×10^{-4} Pa s) T_0 = reference temperature (273.15 K) T = temperature (293.15 K) S = Sutherland constant (110.4 K, at 293.15 K and 1,013 hPa, as discussed in Allen and Raabe 1985)
ρ_p	Particle density	$kg\ m^{-3}$	Assumed to be 1,000 kg m^{-3}
λ_{air}	Mean free path of the air	m	$\lambda_{\text{air}} = \lambda_\circ \times \left(\frac{T}{T_\circ}\right)\left(\frac{P}{P_\circ}\right)\left(\frac{1+S/T_\circ}{1+S/T}\right)$ λo = reference free path (λ_{air} 0.0674×10^{-6} m) at T_0 and P_0 T_0 = reference temperature (273.15 K) T = temperature (293.15 K) P_0 = reference pressure (1,013 hPa) S = Sutherland constant (110.4 K, at 293.15 K and 1,013 hPa, as discussed in Allen and Raabe 1985)

3.5 Local Controls

Evaluation of the effect of local controls can be incorporated by adjusting the emission appropriately. Local controls can include anything from the use of glove boxes to the use of fume hoods. A local control adjustment factor, LC, is applied to the number concentration at the point of emission to allow for these controls.

$$S = S \times \mathrm{LC}. \tag{41}$$

With a current lack of knowledge of the effect of local controls on the levels of nanomaterials, it was decided to base this adjustment factor on those used in the development of the ART model (Table 3).

Table 3 Modifying factors for local controls (Fransman et al. [3])

Type	Classification	Multiplier
No localized control	No localized control	1.0
Suppression technique	Wetting at the point of release	0.1
	Knockdown suppression	0.7
Containment – not extraction	Low level containment (loose lid or cover, which is not air tight)	0.1
	Medium level of containment (sealed process)	0.01
	High level of containment (sealed with valves and enclosed)	0.001
Local ventilation systems-receiving hoods	Canopy hoods	0.5
	Other receiving hoods	0.2
Local ventilation systems-capturing hoods	Fixed capturing hoods	0.1
	Movable capturing hoods	0.5
	On tool extraction	0.1
Local ventilation systems-enclosing hoods (enclosure + LEV)	Fume hood	0.01
	Horizontal downward laminar flow booth	0.1
	Other enclosing hoods	0.1
Local ventilation systems-other LEV	Other LEV	0.5
Glove bags and glove boxes	Glove bag (non-ventilated)	0.01
	Glove bag (ventilated or kept under negative pressure)	0.001
	Low-specification glove box	0.001
	Medium-specification glove box	0.0003
	High-specification glove box	0.0001

3.6 Example

We apply this model to the example outlined in Sect. 2.5.1, assuming a large room of approximately 80 m^3, with an 8 m^3 box (the local control zone, a cube with sides of 2 m). We assume that the source continuously emits nanoparticles at a flow rate of 10 l min^{-1}, at a particle number concentration of 6.3×10^6 cm^{-3}. The corresponding particle size distribution has geometric mean diameter of 61 nm and a geometric standard deviation of 1.72.

Figure 10 illustrates the estimated concentrations in the two zones for two different ventilation rates (2 and 10 exchanges per hour).

At such low concentrations coagulation does not play an important role in the estimated concentrations as the size distribution does not display the shift illustrated in Fig. 1, in fact the ventilation rate is the more important factor in estimating the airborne concentrations with a higher ventilation rate resulting in lower concentrations. Coagulation will have an impact on the estimated concentrations when the emissions are sufficiently high, particularly when ventilation rates are very low.

The levels of ENM that a worker is exposed to can be estimated from these modelled LCIZ and FF concentrations. If the source is constantly in the worker's NF the worker's exposure will be that estimated to be in the LCIZ, and conversely if the source is never in the worker's NF the exposure will be that estimated to be in the FF. With knowledge about the pattern of emission and how the worker moves around the room, and possibly outside it, during a work shift the worker's personal exposure to ENM can be estimated.

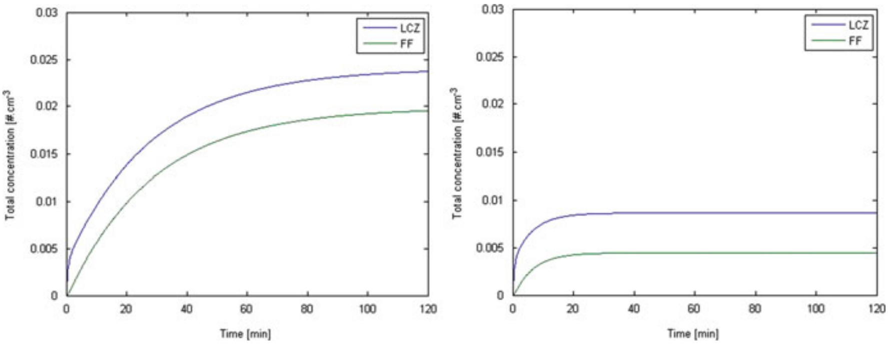

Fig. 10 Estimated concentrations in the local control zone and the far-field given 2 (*left*) and 10 (*right*) air exchanges per hour

4 Discussion

The two exposure models outlined in this chapter are very similar in nature but differ in their complexity. They both account for deposition, diffusion, dilution and coagulation of nanoparticles, using the same principles. The CFD model also accounts for the airflow of the room and allows a complete picture of the expected concentrations at each point in space and time. The two-box model simplifies the space to consist of two boxes to allow for estimation of the concentrations in these two boxes, making the assumption that the concentrations in the two boxes are homogeneous. This assumption is clearly not correct, based on the CFD simulations, but it allows for a quicker, simpler estimation of exposures. The CFD model requires a higher level of expertise, both to program and to run, so while it provides detailed estimation of exposures, it is perhaps beyond the capability of most exposure assessors to implement and run. More importantly, while the CFD model can be applied in situations where conditions are relatively stable, it is not possible to take into account a variety of factors such as moving objects, hot sources, opening doors and windows. Hence in these situations, which will be the case for most accurate occupational scenarios, it will be difficult to program the CFD model to obtain estimates of exposure. More work is required to evaluate whether the assumptions made in the two-box model allow for a reasonably accurate estimation of exposure and under what conditions it performs best.

The output of these models can be used, when information on the emission rate is available, e.g. from simulations or source measurements, to evaluate the exposure levels experienced by workers during their work shift. The models could then be used to evaluate the potential changes in exposure level that would be achieved with alterations to the exposure scenario (i.e. changing room size, ventilation strength, number of sources in the room, use of local control measures). Further to this the outputs of these models could be used in the risk assessment framework, in combination with models for exposure-dose and dose–response, to ultimately estimate the potential that this exposure would have to induce an adverse effect in the worker. The development of the two-box nano-specific exposure model has been developed within the FP7 NANoREG project, with funding from DEFRA, UK.

References

1. Tielemans E, Schneider T, Goede H, Tischer M, Warren N, Kromhout H, Van Tongeren M, Van Hemmen J, Cherrie JW (2008) Conceptual model for assessment of inhalation exposure: defining modifying factors. Ann Occup Hyg 52(7):577–586
2. Marquart H, Heussen H, Le Feber M, Noy D, Tielemans E, Schinkel J, West J, Van Der Schaaf D (2008) 'Stoffenmanager', a web-based control banding tool using an exposure process model. Ann Occup Hyg 52(6):429–441
3. Fransman W, Van Tongeren M, Cherrie J, Tischer M, Schneider T, Schinkel J, Kromhout H, Warren N, Goede H, Tielemans E (2011) Development of a mechanistic model for the Advanced REACH Tool (ART). Ann Occup Hyg 55:957–979

4. Cherrie JW (1999) The effect of room size and general ventilation on the relationship between near and far-field concentrations. Appl Occup Environ Hyg 14(8):539–546
5. Schneider T, Brouwer DH, Koponen IK, Jensen KA, Fransman W, Van Duuren-Stuurman B, Van Tongeren M, Tielemans E (2011) Conceptual model for assessment of inhalation exposure to manufactured nanoparticles. J Expo Sci Environ Epidemiol 21:450–463
6. Koivisto AJ, Yu M, Hämeri K, Seipenbusch M (2012) Size resolved particle emission rates from an evolving indoor aerosol system. J Aerosol Sci 47:58–69
7. Shih TH, Liou WW, Shabbir A, Yang Z, Zhu J (1995) A new k-epsilon Eddy-viscosity model for high Reynolds number turbulent flows - model development and validation. Comput Fluids 24:227–238
8. Yakhot V, Orszag SA, Thangam S, Gatski TB, Speziale CG (1992) Development of turbulence models for shear flows by a double expansion technique. Phys Fluids A 4(7):1510–1520
9. Posner JD, Buchanan CR, Dunn-Rankin D (2003) Measurement and prediction of indoor air flow in a model room. Energy Build 35(5):515–526
10. Chen F, Yu SCM, Lai ACK (2006) Modeling particle distribution and deposition in indoor environments with a new drift–flux model. Atmos Environ 40(2):357–367
11. Elghobashi S (1994) On predicting particle-laden turbulent flows. Appl Sci Res 52:309
12. Barbe-Le Borgne M (1987) Étude expérimentale et théorique de la coagulation des aérosols liquides, PhD. Thesis, Paris XII, 1987
13. Gao N, Niu J (2007) Modeling particle dispersion and deposition in indoor environments. Atmos Environ 41(18):3862–3876
14. Holmberg S, Chen Q (2003) Air flow and particle control with different ventilation systems in a classroom. Indoor Air 13(2):200–204
15. Holmberg S, Li Y (1998) Modelling of the indoor environment – particle dispersion and deposition. Indoor Air 8(2):113–122
16. Zhao B, Li X, Zhang Z (2004) Numerical study of particle deposition in two differently ventilated rooms. Indoor Built Environ 13(6):443–451
17. Zaichik LI, Soloviev SL, Skibin AP, Alipchenkov VM (2004) A diffusion-inertia model for predicting dispersion of low-inertia particles in turbulent flows. In: Proceedings of the 5th international conference on multiphase flow, Yokohama
18. Gimbun J, Nagy ZK, Rielly CD (2009) Simultaneous quadrature method of moments for the solution of population balance equations, using a differential algebraic equation framework. Ind Eng Chem Res 48(16):7798–7812
19. Guichard R, Tanière A, Belut E, Rimbert N (2014) Simulation of nanoparticle coagulation under Brownian motion and turbulence in a differential–algebraic framework: developments and applications. Int J Multiphase Flow 64:73–84
20. Marchisio DL, Fox RO (2013) Computational models for polydisperse particulate and multiphase systems. Cambridge University Press, Cambridge
21. McGraw R (1997) Description of aerosol dynamics by the quadrature method of moments. Aerosol Sci Tech 27(2):255–265
22. Yu M, Lin J (2009) Taylor-expansion moment method for agglomerate coagulation due to Brownian motion in the entire size regime. J Aerosol Sci 40(6):549–562
23. Marchisio DL, Pikturna JT, Fox RO, Vigil RD, Barresi AA (2003) Quadrature method of moments for population-balance equations. AIChE J 49(5):1266–1276
24. Guichard R, Tanière A, Belut E, Rimbert N (2013) Modelling of nanoparticle coagulation and transport in pipe flow. Int J Vent 12(2):181–186
25. Guichard R, Tanière A, Belut E, Rimbert N (2013) Modeling coagulation, transport and deposition of a nanoparticle aerosol by a moment method. In: Proceedings for the 8th international conference on multiphase flow, Jeju
26. Friedlander SK et al (2000) Smoke, dust, and haze, vol 198. Oxford University Press, New York
27. Zaichik LI, Solov'ev A (2002) Collision and coagulation nuclei under conditions of Brownian and turbulent motion of aerosol particles. High Temp 40(3):422–427

28. Vanni M (2000) Creeping flow over spherical permeable aggregates. Chem Eng Sci 55 (3):685–698
29. Saffman P, Turner J (1956) On the collision of drops in turbulent clouds. J Fluid Mech 1 (01):16–30
30. Smoluchowski M (1917) Versuch einer mathematischen Theorie der Koagulationskinetik kolloider Lösungen
31. Petzold LR (1982) A description of DASSL: a differential/algebraic system solver. In: Proceedings of IMACS World congress, Sandia National Laboratories, Livermore, USA, pp 430–432
32. Nerisson P, Simonin O, Ricciardi L, Douce A, Fazileabasse J (2011) Improved CFD transport and boundary conditions models for low-inertia particles. Comput Fluids 40(1):79–91
33. Guichard R, Belut E, Rimbert N, Tanière A (2014) Evaluation of a moments-based formulation for the transport and deposition of small inertia aerosols. J Comput Multiphase Flows 6 (4):407–418
34. Maynard AD, Zimmer AT (2003) Development and validation of a simple numerical model for estimating workplace aerosol size distribution evolution through coagulation, settling, and diffusion. Aerosol Sci Technol 37(10):804–817
35. Seinfeld JH, Pandis SN (1998) Atmospheric chemistry and physics. Wiley, New York
36. Allen MD, Raabe OG (1985) Slip correction measurements of spherical solid aerosol particles in an improved Millikan apparatus. Aerosol Sci Tech 4:269–286

The Flows of Engineered Nanomaterials from Production, Use, and Disposal to the Environment

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Abstract The aim of this chapter is to evaluate what information is needed in order to quantify the flows of ENM to the environment by reviewing the current state of knowledge. The life cycle thinking forms the basis of the evaluation. The first step in release assessment is the knowledge about the production and use of ENM. Data on production are crucial for the assessment, because they determine the maximal amount that could potentially be released. The different life cycles of products containing the ENM are determining the release potential. The knowledge about the product distribution is therefore key to release estimation. The three important life cycle steps that need to be considered are production/manufacturing, the use phase, and the end of life (EoL) treatment. Release during production and manufacturing to the environment may occur because large amounts of pure material are handled. During the use and EoL phase, experimental data from real-world release studies are preferred; however, in most cases release has been estimated or guessed based on standard knowledge about product use and behavior. The mass flows discussed in this chapter provide the input data to derive environmental concentrations needed for environmental risk assessment of ENM. The mass flows to the environment will also be needed for environmental fate models that are based on mechanistic

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description of the reactions and the behavior of the released ENM in environmental compartments such as water or soils.

Keywords Nanomaterials, Life cycle perspectives, Release, Material flow modeling

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1 Introduction

The assessment of the environmental exposure to engineered nanomaterials (ENM) is still an area with limited information available. An ENM in the context of this chapter means any intentionally manufactured material, containing particles, in an unbound state or as an aggregate or as an agglomerate and where, for 50% or more of the particles in the number size distribution, one or more external dimensions is in the size range 1–100 nm [1]. The direct measurements of ENM at environmentally relevant concentrations are currently not possible with the existing analytical techniques [2, 3], and thus modeling is the only way to estimate environmental exposure concentrations. Nevertheless, we have sufficient information to conclude that environmental exposure to ENM is a reality and that numerous materials are actually present in the environment [2, 4]. However, quantitative information on the flows from products to the environment is still very scarce. This is due to the limited knowledge on the actual use of nanomaterials in products and processes and the dearth of investigations on release under real-world conditions. Within this chapter we combined the information available in the literature about production amounts, distribution to products, and release from products and to present the currently available mass flow models that quantitatively describe the flows of ENM from production to the environment. These mass flow data are needed as inputs to environmental fate models that are able to provide environmental concentrations of ENM, e.g., predicted environmental concentrations (PEC) values, needed for risk assessment.

The approach is based on the life cycle of production, manufacturing, use, and release (see Fig. 1). The knowledge about the production and use of ENM stands at

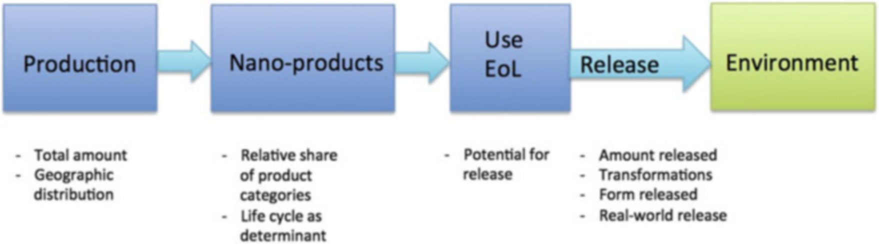


Fig. 1 Life cycle steps where information needs to be obtained in order to assess the flows of nanomaterials to the environment: production, distribution to product categories, and release. These steps are discussed in detail in this report. The *arrows* indicate information and not material flow. *EoL* end of life

the beginning of the exposure assessment. Data on production are crucial for exposure assessment, as they determine the maximal amount that could potentially be released. The life cycle of products is determining the potential for release, and thus knowledge on the actual product distribution is paramount to any exposure estimation [5]. The two important life cycle steps that need to be considered are the use phase and the end of life (EoL) treatment. The next steps are then investigations on actual release from products, preferably under real-world conditions so that finally the mass flows to the environment can be quantified. In addition release during production and manufacturing may occur, which is mainly of relevance for occupational exposure but also constitutes a possible release pathway to the environment. These aspects will be discussed in detail in this chapter, and the current knowledge that is available to enable quantifying the flows of ENM to the environment will be presented. Finally a toolbox is presented that allows in a systematic way to assess the flows of ENM to the environment.

The mass flows discussed in this chapter provide the input data to derive environmental concentrations. The mass flows to the environment will also be needed for environmental fate models that are based on mechanistic description of the reactions and the behavior of the released ENM in environmental compartments such as water or soils.

2 Production Amounts

When industry is approached for production volumes of ENM, the general reluctance of industry to reveal business-sensitive information is further aggravated by two nano-specific uncertainties: First, the legal framework in Europe and elsewhere currently undergoes a dynamic development. The future regulatory requirements for ENM are highly uncertain, but might incur costs that can easily nil the profit margin of specialty grades (low production volume nano-forms).

Second, the internal databases of companies specify chemical identity and performance criteria, but “novel,” “engineered,” “intentional,” or number metrics are not part of the specifications. The coexistence of differently sized forms of same chemical composition and the technical irrelevance of size for intermediates (here: particulate chemicals that perform after dissolution or melting) make it challenging to decide which is to be considered as ENM. The fact that national inventories (France 2014, Belgium 2015, Denmark 2015) each carve out different materials from the overarching EC definition and from applicable legal frameworks (Cosmetics directive 2012, Food directive 2014, REACH Annexes expected in 2015) does not contribute much to transparency within and between companies.

As a consequence, little is known about production amounts of ENM on a quantitative level, e.g., tons/year produced in different regions. We need to consider differentiating between amount of "production," "manufacturing," and "consumption." The produced amount of ENM in one region, the ENM manufactured in products, and the amount of products consumed in one region are all different. So far this aspect has not really received a lot of attention, and production and consumption are used interchangeably, mainly due to the absence of basic data. Very few scientific papers are actually providing data about production/consumption volumes. One of the earliest reports is from Schmid and Riediker [6] who provided quantitative production data based on a survey of the Swiss industry. Hendren et al. [7] provided an in-depth evaluation of production of five ENM in the USA. By using a variety of sources, companies producing ENM in the USA were identified and production volumes determined. Piccinno et al. [8] reported the results from a survey of companies producing and using ENM about the estimate of the worldwide/Europe-wide production amounts. In this work quite a spread of answers was obtained, most probably indicative of problems related to the definition of ENM. This work was conducted before the EC definition of "nanomaterial" was released [1]. For some materials such as nano-SiO_2, there is a huge spread in reported amounts, reflecting conflicting replies from different experts, part of whom considered a certain form of chemicals as ENM, whereas the other part considered this form as conventional chemical. This discrepancy is also visible in some higher estimated European compared to worldwide production amounts. Keller et al. [9] have used for their modeling of ENM flows a commercially available report as basis for the ENM production data [10]. The production values were taken as reported by FutureMarkets and no uncertainty range is provided. Worldwide production amounts for ten different ENM are presented in this work.

Another source reporting production amounts is the recent evaluation of nanomaterial registrations from France [11]. The highest production/use amounts (carbon black and silica) are those of conventional materials that fall under the French Decret definition of a nanomaterial (which is the same than the EU-definition [1]). The compiled list provided in the ANSES report only contains materials with more than 100 tons/year production/import. Silver was only reported for scientific research with a mass of 0.1–1 kg in the detailed lists provided in the report. With more than 3,000 registrations, the registry is clearly the most exhaustive compilation on production and use of nanomaterials, so it is very reasonable to assume that indeed almost no nano-Ag is imported or produced in France. Import in final products (e.g., textiles) was not covered by the register.

Table 1 Comparison of production amounts from six different sources scaled to the EU (according to the GDP) (in tons/year)

ENM	Schmid and Riediker [6]	Hendren et al. [7]	Piccinno et al. [8]	Keller et al. [9]	ANSES [11]	Sun et al. [12]
TiO_2	11,500	8,600–42,000	550	20,000	92,000	10,000
Ag	82	3–20	6	100	0.006	30
ZnO	1,900	–	55	7,900	1,900	1,600
CNT	26	60–1,200	550	740	–	380
C_{60}	–	2–90	0.6	–	<100	20
CeO_2	–	40–770	55	2,300	700	–
Al-ox	0.1	–	550	8,100	15,000	–
Fe-ox	9,700	–	550	9,700	6,100	–
SiO_2	2,000	–	5,500	22,000	990,000	–
Nanoclays	–	–	–	2,400	<100	–
Cu	–	–	–	46	<100	–
Quantum dots	–	–	0.6	–	–	–

In Table 1 the production amounts from the six sources mentioned above are compared on the basis of a scaling of the original estimates to the EU based on the gross domestic product (GDP). This scaling procedure has been used by several authors to scale production data from one region to another [12, 13]. Using this approach data obtained for different regions can be directly compared.

For nano-TiO_2 and Ag, all six sources provide production data, and for nano-ZnO and CNT, five sources provide data. A comparison of the data in Table 1 shows significant differences between the values from some sources with factors for most materials in the range from two to five and up to 45 for nano-SiO_2. For most nanomaterials, there is a general agreement on the order of magnitude of production, so $TiO_2 > ZnO > CNT > Ag > C60$. The largest variability is observed for materials that are also produced in conventional form, e.g., all the metal oxides such as SiO_2, Fe-oxides, and Al-oxides. For these materials a major problem associated with production amounts is clearly to define when a certain material is considered an ENM and when a conventional material. The very high production of nano-SiO_2 reported in the French ANSES registry clearly includes what in many other sources might be considered non-nano silica. Also for TiO_2 the value obtained from the French source is much higher than all the other values, and a similar issue might also play a role here. Worldwide production of pigment TiO_2 is more than four million tons [14]. However, we also have to consider that the values in Table 1 have been extrapolated in many cases to the EU based on the GDP.

Sun et al. [12] have combined the available information on production of ENM and have obtained probability distributions for five ENM (see Fig. 2). Two of the sources mentioned above, the ANSES report and Keller et al. [9], were published later and were not included in the evaluation. Sun et al. [12] classified the available data according to source of the data and considered some data to be of higher quality than others (e.g., peer-reviewed studies scored higher than reports without

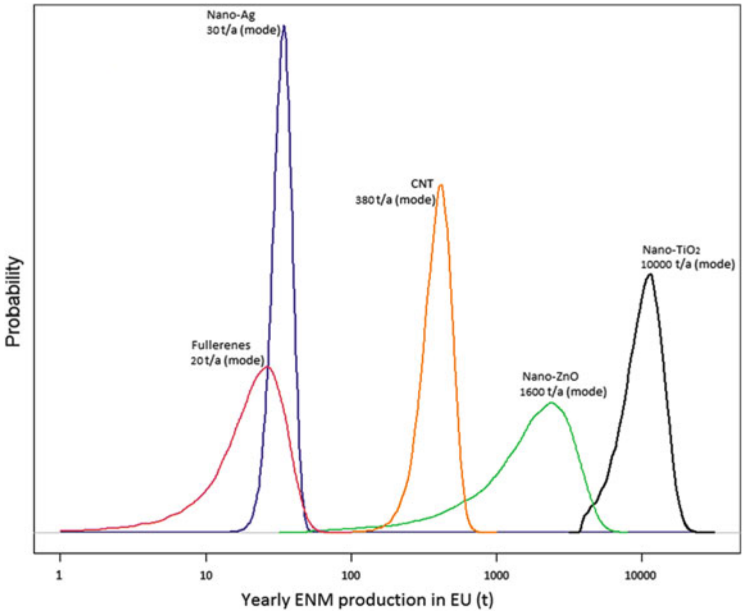


Fig. 2 Yearly production/use of five ENM in the EU. Shown are the probability distributions for fullerenes, nano-Ag, CNT, nano-ZnO, and nano-TiO_2 by considering data from a variety of sources. Figure taken from Sun et al. [12]

information on the methods that were used). Figure 2 shows that of the covered ENMs (TiO_2, ZnO, Ag, CNT, C_{60}), the largest production is that for nano-TiO_2 with a production in the EU of about 10,000 tons/year, followed by nano-ZnO with about 1,600 tons/year and CNTs with 380 tons/year. Nano-Ag with 30 tons/year and fullerenes with 20 tons/year have only low production amounts. These values are the mode values (most likely value) from the probabilistic assessment; the shape of the curve represents the current level of uncertainty.

3 Product Distribution

Whereas on production amounts at least some information has been published as was shown in the previous section, almost no quantitative information is available on the distribution of the produced ENM amount to different product categories. A lot of the knowledge we have about products stems from inventories such as the Woodrow Wilson Inventory [15], but such inventories have substantive deficiencies [16]. The main deficiency is that they just list articles claiming to contain ENM without proof that they actually contain an ENM; also information on concentrations of ENM in the products is seldom given. Many papers and reports list possible application areas of ENM [17–19], but this is only qualitative information that tells

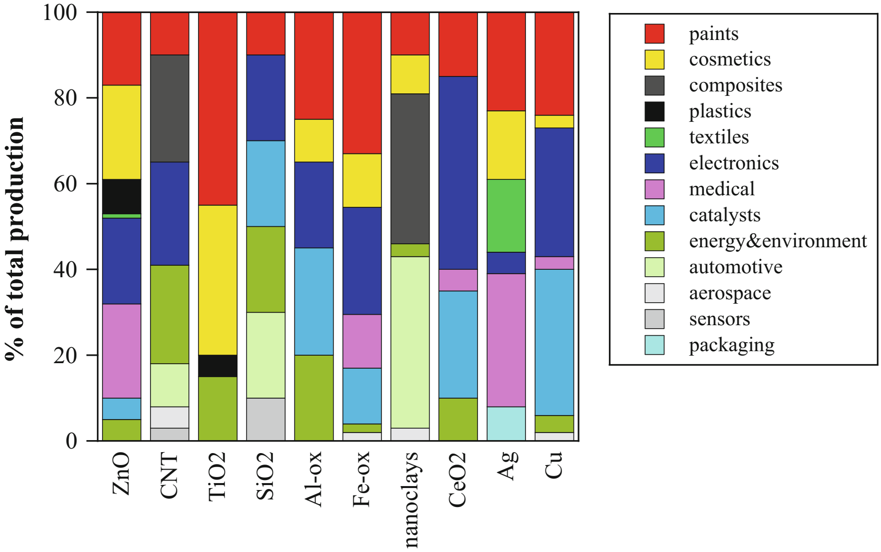


Fig. 3 Product distribution adapted from Keller et al. [9] in % of the total production of the ENM

us in which products an ENM might be used but not how important this product category is in terms of the share of the total ENM production that is used. What we need are data on the distribution of the produced ENM amount to different product categories.

Piccinno et al. [8] performed a survey among industries producing or using ENM and obtained some quantitative information on the distribution of the production amount to different product categories. The replies refer to the percentage of the total production that is used in certain product categories.

Keller et al. [9] used the FutureMarkets report not only as source of production amounts but also to get data on the product distribution. As with the production data, Keller et al. [9] did not further evaluate the data from the FutureMarkets report but used them as they were reported. Figures 3 and 4 present the distribution of the production for the different ENM to various product categories that we extracted from the mass flow data presented in the paper. In Fig. 3 the data are shown in relative amounts for each of the ten investigated ENM; in Fig. 4 the absolute amounts are given.

Sun et al. [12] combined the available information to derive best estimates of product distribution. Figures 5 and 6 show the relative and absolute product distribution for five ENM and pigment TiO_2.

One difficulty in comparing the results from these three data sources is that the used product categories are different. Sun et al. [12] used product categories mainly based on similar life cycles, whereas some other sources used also categories based on technical sectors. In the automotive sector, many ENM are used either in polymer composites or in electronic parts. For a quantitative estimation or even

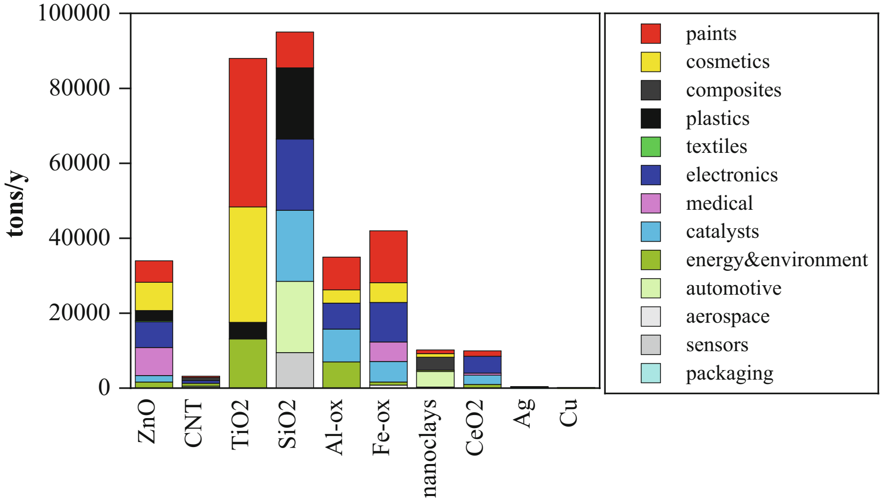


Fig. 4 Product distribution adapted from Keller et al. [9] in absolute amounts (tons/year) for the different ENM

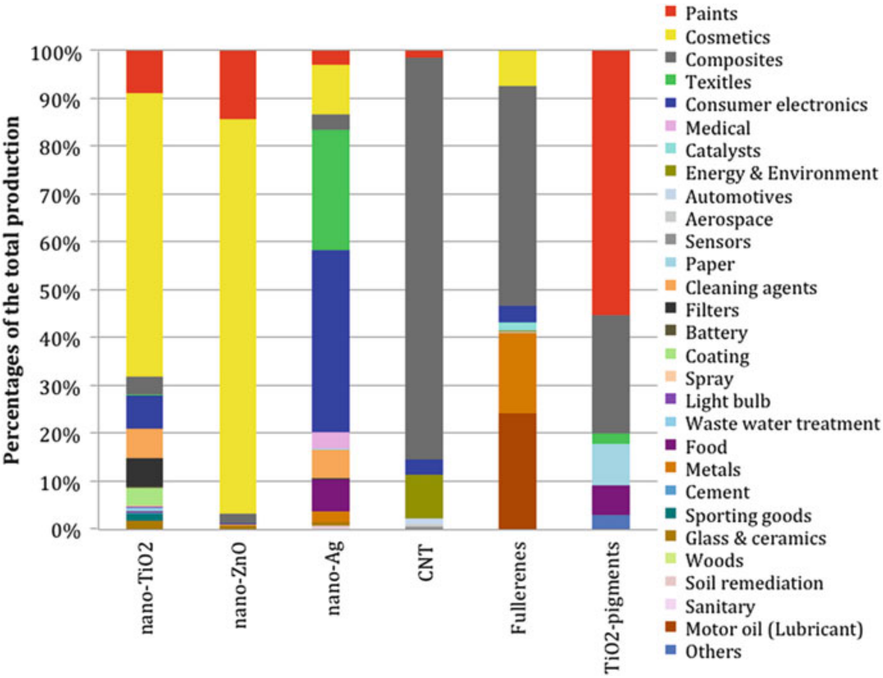


Fig. 5 Product distribution for 5 ENM and pigment TiO_2 adapted from Sun et al. [12]. The values are derived by combining various sources to obtain a "best estimate"

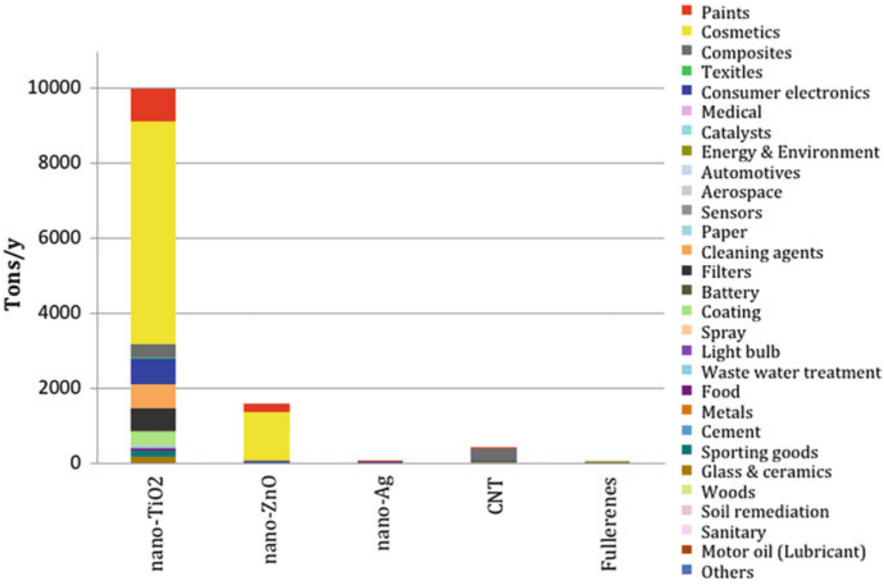


Fig. 6 Product distribution used absolute amounts for the different ENM adapted from Sun et al. [12]

modeling of ENM flows, these data, together with the production amount, form the basis for any flow estimation or model. The knowledge about the product categories can directly be used to estimate the potential for release, as shown in the next section.

4 Potential for Release

The knowledge about the products that contain ENMs can be used in a life cycle perspective to evaluate the potential for release [5]. Such an evaluation has been performed by Nowack et al. [20] to assess the exposure potential from ten technology sectors for workers, consumers, and the environment. The exposure was rated with four levels from “unlikely” over “low” and “medium” to “high.” The main pathways of potential environmental release across the life cycle that were identified in this work were:

- Release of free ENM used during manufacturing into waste streams and air
- Intentional or unintentional release during product use
- Release during disposal or recycling of the product, mainly if this involves shredding or combustion processes

Such a qualitative evaluation can be used as starting point for further exposure evaluations and to guide research to areas where release and exposure can be

Table 2 Release potential for CNTs used in polymers

Release scenario	Professional user	Consumer	Environment	Recycling
Injection molding	Unlikely	–	Unlikely	–
Manufacturing	Very likely	–	Unlikely	–
Sports equipment	–	Unlikely	Very unlikely	Likely
Electronics	–	Unlikely	Unlikely	Likely
Windmill blades/ fuel system parts	–	Very unlikely	Unlikely	Likely
Tires	–	Very likely (through environment)	Very likely	Likely
Textiles		Very likely	Very likely (through wastewater)	Likely
Incineration	–	–	Unlikely	–
Landfill	–	–	Unlikely	–

Modified from Nowack et al. [21]
–: not applicable (life cycle stage not considered in scenario)

Table 3 Possible release mechanisms of ENM for different product categories

Product category	Release mechanism	Environmental compartment	Release potential
Cosmetics	Application of product	Water, wastewater	100%
Medical uses	Application of product	Wastewater	100%
Food	Application of product	Wastewater	100%
Water treatment, remediation	Direct release	Water, soil	100%
Sprays	Direct release	Air	100%
Textiles	Washing	Wastewater	High
Paints, coatings	Application of product Weathering, photodegradation	Air, water, soil	Moderate
Food packaging	Leaching	Food, wastewater	Low
Composites, plastics	Abrasion, weathering, photodegradation	Air, soil	Low
Tires	Abrasion	Air, soil	High
Electronics, batteries	Recycling, disposal	Air, wastewater	Low
Automotive/ aerospace	Recycling, disposal	Air, wastewater	Low

expected to occur. In this assessment the starting point was the technology sector and not product category.

A similar assessment was also performed for CNTs contained in polymers, see Table 2. Again the life cycle perspective approach was chosen in order to identify product types with significant release potential. The use in tires and textiles was

Table 4 Published release studies with ENM and actual products: model and real-world studies, excluding studies with lab test without relevance to real products (e.g., by "washing" or leaching with distilled water)

Product type	ENM	Model study	Real world	Reference
Textiles	Ag	Washing test		[22]
	Ag	Washing test		[23]
	TiO_2	Washing test		[24]
	Ag		Home washing	[25]
	Ag		Release from washing machine	[26]
	Ag		Direct release to environment	[27]
Paints	Ag		Model house	[28]
	TiO_2	Climate chamber		[29]
	SiO_2	Climate chamber		[30]
Wood coating	Ag		Outdoor weathering	[31]
Food containers	Ag	Leaching tests		[32]
	Ag	Leaching tests		[33]
	Ag	Leaching test		[34]
	Ag	Leaching tests		[35]
Polymer composites	CNT	Weathering tests		[36, 37]
	SiO_2	Weathering tests		[38]
Sprays	Ag	Spray chamber		[39]
	ZnO/Ag	Spray chamber		[40]
Sunscreens	TiO_2	Model water		[41]
	TiO_2		Bathing lake	[42]
	TiO_2		Swimming pool	[43]

identified to result in likely release, and also recycling operations were found to be highly likely sources of released particles to the environment.

The release potential evaluations are possible to be carried out because in a certain product type only a limited number of release mechanisms will play a role. The mechanisms of release from products are not nano-specific but are determined by the environment the product is used in, the forces that act upon it, and the way it is used. For pure ENM, e.g., powders, the fact that they are nano influences the release, but this is more relevant for occupational exposure than for release to the environment during product use. In Table 3 the most relevant release mechanisms for the different product categories covered in this report are listed.

It is clear from looking at Table 4 that different product categories have completely different release potential. It is also important to note that in most cases material release will be into a technical compartment (wastewater treatment plants, waste incinerations plants, landfills) where most of the ENM will be removed and are not released to the environment. There are many product categories where no or only a very small release is expected during use but where release might occur during disposal or recycling. This stage is therefore of utmost importance for evaluating ENM flows. However, the modeling of ENM flows during waste handling has shown that only minor releases are expected to the environment, major flows are going into different types of landfills [44]. The fate of ENM during recycling operations is still unknown, but first results are expected to come out from the SUN project soon.

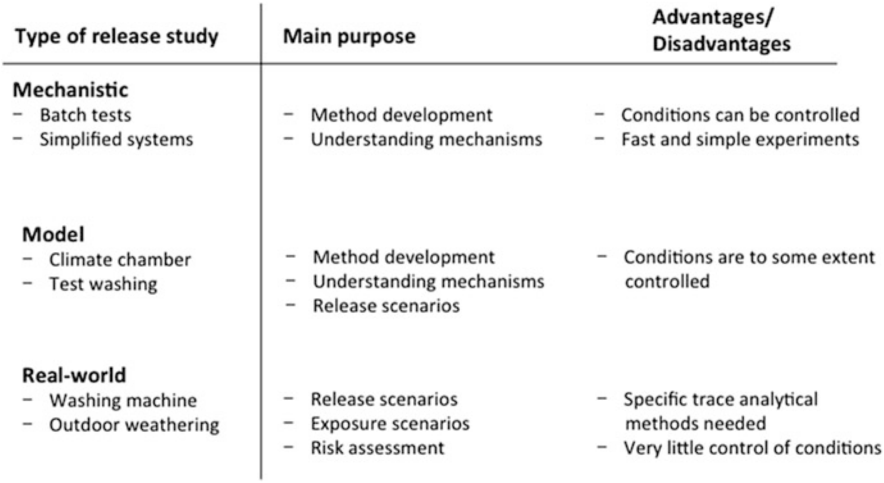
5 Release Experiments of ENM During Use

In the previous section, the potential for release was covered. In this section studies that actually measured release of ENM from products are discussed. Recently a few reviews on this topic have been published. Froggett et al. [45] have reviewed the data on release of materials from solid nanocomposites. They state that very little attention has been focused so far on understanding the conditions for release of ENM from nanocomposites. They identified studies that investigated the release of ENM and reviewed them according to various release scenarios: machining, weathering, washing, contact, and incineration. The materials released from nanocomposites contain a mixture of four types of (1) particles of matrix alone and, slightly less often, the (2) matrix particles with the nanomaterial partially or fully embedded; far less frequently is the added nanomaterial entirely dissociated from the matrix identified, and most rare are (4) dissolved ionic forms of the added nanomaterial. However, depending on the nanomaterial, dissolution can be a major process during aging/release. Some textile release studies have found significant release of dissolved silver [46, 47].

Nowack [48] discussed the different types of release studies (see Fig. 7). This figure compares the different types of release studies and lists the possibilities and advantages of them. All studies have their merits and ideally data from all three levels are available, allowing us to understand the mechanisms as well as having data that can be used for exposure scenarios.

Release studies can be performed at different levels of complexity. At the basic level, experiments with simplified and standardized test materials allow controlling the physical and chemical conditions of the release. These tests are therefore suitable to investigate the mechanisms of release and to develop new experimental and analytical methods. The results from these studies may have only a limited value in estimating the amounts of nanomaterials released in the real world.

At the next level of complexity, studies are performed that mimic the real world but are still carried out under controlled conditions. Examples include tests with laboratory washing machines to study release from textiles or the use of weathering chambers to investigate release from paints. In these tests more parameters are fixed but still a sufficient control over the chemical and physical conditions is possible. However, because the tests are performed on a larger scale, the number of replicates or treatments is more limited. Very often these tests are based on established



Type of release study	Main purpose	Advantages/ Disadvantages
Mechanistic – Batch tests – Simplified systems	– Method development – Understanding mechanisms	– Conditions can be controlled – Fast and simple experiments
Model – Climate chamber – Test washing	– Method development – Understanding mechanisms – Release scenarios	– Conditions are to some extent controlled
Real-world – Washing machine – Outdoor weathering	– Release scenarios – Exposure scenarios – Risk assessment	– Specific trace analytical methods needed – Very little control of conditions

Fig. 7 Classification of release studies. Figure modified after Nowack [48]

standards or norms, and thus certain parameters are fixed according to the standard. An example is the use of ISO washing tests for color fastness that were adapted to investigate release of nano-Ag from textiles [22]. In order to be able to collect the released materials and to guarantee sufficiently low levels of silver background, several adaptations were made. Although these release studies are not directly transferable to the real world, they provide information that allows estimation of the order of magnitude of a certain release as well as the characterization of the released materials.

The highest level of relevance for understanding release under real-world conditions are studies performed under normal use of products. This could be to follow weathering and release of materials from facades painted with nano-paints or washing of clothes in normal washing machines. However, the exposure conditions are much less controlled. When a single nano-T-shirt is washed together with several kg of other textiles in a normal washing machine, the quantification and characterization of the released materials in several liters of washing and rinsing liquid is very difficult, if not impossible. The released ENMs are diluted to a large extent and occur together with a large variety of other materials released from the various textiles. In the lab washing machine, the solid/water ratio and the amount of textiles can be optimized to allow detection of released materials under the chosen analytical methods. However, if performed well, real-world studies provide data that can be directly used for environmental release and exposure scenarios.

6 Environmental Release from Occupational Settings

Nanomaterials that enter an occupational setting leave the workplace in normal circumstances either as pure ENM, inside a product, by general or special waste collection, by wastewater, or by natural or artificial air ventilation. Some ventilation systems will be equipped with filters, in which case the material will end of in solid or special waste. Cleaning and maintenance activities (including those involving nanomaterials) will in most cases lead to nanomaterials reaching both wastewater and general or special waste. Some nanomaterials may also accumulate within the facilities and will be removed only during major renovation activities. These may end up, in principle, also on landfills. In the case of accidents or fires, nanomaterials may be released in larger amounts into the air and into natural waters in cases where there are no detention basins in place to collect excessive amounts of fire-extinguishing water.

Little information is available on environmental release from occupational settings. These settings are:

- Production of nanomaterials
- Manufacture of intermediates/products containing nanomaterials
- Professional use of products containing nanomaterials

The focus of occupational studies is usually production processes involving nanomaterials and their relation to workers exposure. Most studies aim to answer either how much nanomaterial gets released into the work space or what concentrations workers experience during their work shift or during specific tasks and activities. Release of ENM from occupational settings to the environment could be addressed following a life cycle approach. The evaluation of each activity across the life cycle together with the risk management measures and cleaning practices used for such activities would provide an insight on the likelihood of release. However, technical protection measures such as encapsulations and ventilation systems strongly affect release into indoor environments and workers' exposure, and thus ventilation data is frequently collected. By combining ventilation flow data with concentration measurements in the exhaust flow, one can estimate the release into the outdoor environment. For nanomaterials that are used for cleaning purposes, one can obtain an initial estimate by assuming that most of the material used will eventually end up in the wastewater and be transported to a wastewater treatment plant (at least in most developed countries). For accidental or fire scenarios, one can assess the quantities stored on site to obtain worst-case release numbers.

Release by waste disposal has also to be accounted, not only for ENM intentionally used for cleaning but also for the ENM collected from cleaning instruments, laboratory material, spills, etc., usually end up in the general waste bin.

In the scientific literature, information about treatment methods for material wastes such as ventilated air or water that leaves a washing process is usually not described. Thus, most of the materials will be released into the environment or will be captured by an exhaust filter, depending on the safety measures at each workplace. In many chemical fume hoods, there is no retention system and related rules differentiate by countries. For example, industrial processes usually include exhaust gas treatment processes such as filtration or burning off (in the case of high VOC content). In most of the cases, airborne particles are found to be emitted during the manufacturing and handling processes. Ventilation systems are used to control potential exposures, such as laboratory fume hood, local exhaust ventilation (LEV), natural ventilation (door, window), rooftop fan, and central ventilation.

When LEV is not used and the only air exchange is with outdoor air, the concentration of nanomaterials released to the environment could be estimated from the indoor concentration and the ventilation flow rate. However, published papers do not often include quantitative data on ventilation flow rates. In a study conducted in a laboratory with only general mechanical ventilation, the rate of 1 room exchange per hour was reported [49]. No direct air exchange through windows or doors was possible (there were no windows and the main door was kept closed during the experiments). The source and personal breathing zone (PBZ) particle concentrations were measured. In this case, one way to estimate the environmental release flow can be first to calculate the room average particle concentration from the source and PBZ data by using transport or diffusion kinetics (e.g., near-field/far-field two zone model) and then combine it with the room volume and air change rate (ACH) to estimate the final mass flow rate to the environment. This is, however, only possible if the air exchange is with outdoor air and there are no local controls such as LEV. Another study reported an ACH of 2–10 per hour in research laboratories of particle synthesis [50]. In one of their previous studies, an ACH of 0.706/h was also given in an industrial pilot plant [51]. In this study, a one-box model based on particle number conservation was employed to estimate particle emission rate from the average number concentration profile. This data can then be directly used for the calculation of environmental flow rates. In the cases where natural ventilation are employed [52–54] such as doors and windows, the room ACH can be calculated if wind speed and total area of open surfaces are available. There are also references on typical ACHs if these data are not directly given, such as handbooks (Exposure Factors Handbook, EPA; 2011) and scientific publications [55–57].

When exhaust ventilation is used (without filters), then the exhaust flow rate and concentration at the exhaust can be used to estimate the release of nanomaterials.

7 Release Data and Mass Flows

The main aim of this chapter is to derive mass flows from products to the environment. So the final goal is to have flows in mass/time unit for the use phase of the product, either for one unit of the product or for all products used within a certain region. Preferably population-normalized values, e.g., mass/time/capita, should be available, allowing a simple adaptation of the total release in different regions based on population. Unfortunately, often release data have units of mass/volume of leachate or mass/surface area exposed. The mass/volume data are useful to prove that release takes place and understand the mechanisms, but are less useful for deriving mass flows. Critical issues when using such data for deriving mass flows are:

- How to extrapolate a short-term experiment to years of use (release kinetics, aging)
- How to convert mass/volume to mass/product

An additional issue is that release data are often not nano-specific, so they do not provide sufficient characterization of the released materials in real-world studies. For example, textile studies reporting only release of Ag are not really useful to estimate the flows of nanomaterials because only a fraction of the silver release from textiles is still in the original nano-form [58]. Significant dissolution and transformation was observed, with only a small fraction still present in original nanoparticulate form. There were also significant nanoparticulate fractions observed in the washing liquid of conventional silver textiles, further complicating the assessment of release of nanomaterials. Such total release measurements can be used to derive the total flows originating from nanoproducts but not to quantify the nanomaterial flows. However, so far only very few studies have actually characterized quantitatively the released materials so that mass flows of nanoparticulate releases can be distinguished from other releases.

8 Review on Mass Flows of ENM to the Environment

Several studies are available that modeled mass flows from products to the environment. These studies collated the available information and derived mass flows, using different approaches. These models have already been reviewed with respect to the type of model and the advantages and disadvantages of the different approaches [4, 59]. In this chapter only the mass flow result from these studies is discussed and compared.

The most recent and most complete study has been published by Sun et al. [12]. This work is based on the predecessor models of Mueller and Nowack [60] and Gottschalk et al. [61]. Figure 8 shows an example of the material flow diagrams that were published in that work. It shows the yearly flows of nano-TiO_2 in the EU originating from production, manufacturing, and use to the technical systems (e.g., wastewater treatment, waste incineration) and finally to the environment. Such flows were calculated for nano-TiO_2, nano-ZnO, nano-Ag, CNT, and fullerenes. The flows correspond to total nano-flows, irrespective of the form the particles have (e.g., single, agglomerates, attached to larger particles). Transformation, e.g., dissolution or sulfidation, was included for some materials, resulting in flow into an elimination compartment.

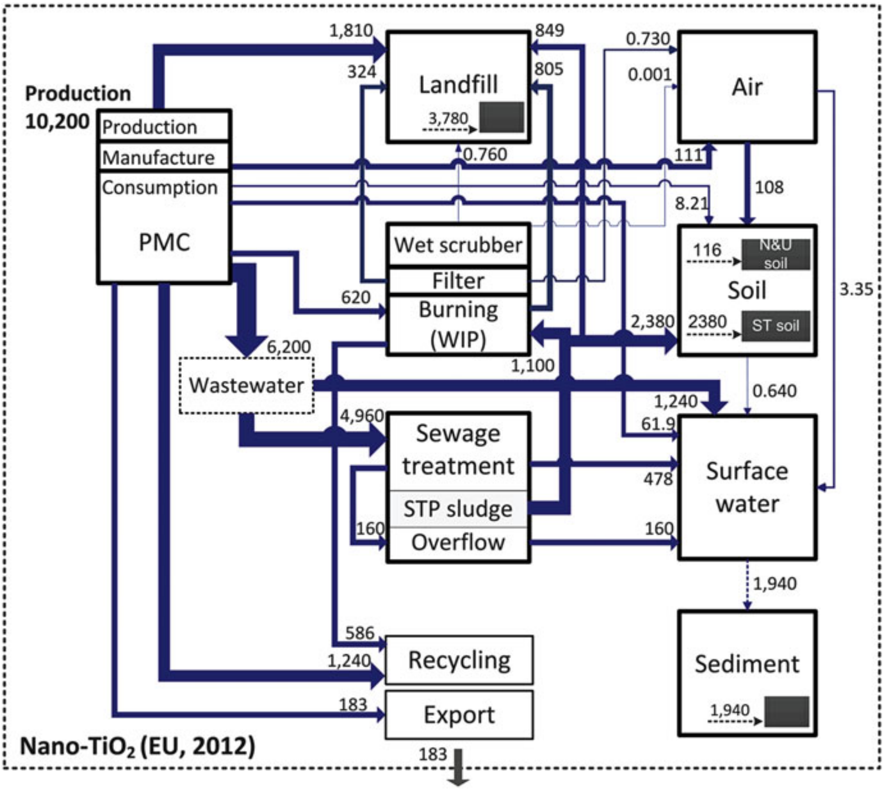


Fig. 8 Material flow model for nano-TiO_2 from production/manufacturing/use to the environment in EU in 2012. Figure taken from Sun et al. [12]

Table 5 Mass flows to the environment (and landfills)

ENM	Wastewater	Water	Sludge-treated soil	Soil (diffuse)	Air	Landfill
TiO_2	6,200	1,940	2,380	116	112	3,780
Ag	8.85	2.1	0.42	0.84	0.52	5.2
ZnO	1,050	328	0.006	10.6	8.2	300
CNT	1.9	0.71	0.77	3.6	3.7	190

Data based on Sun et al. [12]. Values in tons/year in the EU

Table 5 provides the mass flows for four nanomaterials summed up for different environmental compartments. These mass flows can then be converted into environmental concentrations using established procedures [62]. Sun et al. [12] also provide ENM concentrations in technical systems, e.g., wastewater, municipal waste, and waste incineration slag and filter ash. These concentrations provide the currently most advanced estimates of environmental exposure to the five studied materials.

Table 6 Mass flows to the environment (and landfills) in the EU

ENM	Water	Soil	Air	Landfill
TiO_2	3,600	8,900	370	7,600
Ag	15	35	3	46
ZnO	860	2,000	140	4,900
CNT	8	120	10	630

Data based on Keller et al. [9], values extrapolated to Europe based on GDP, in tons/year

Keller et al. [9] provide similar material flow diagrams for ten different materials. However, whereas Sun et al. [12] use probabilistic modeling, incorporating the variability and uncertainty of the input values, Keller et al. [9] use only one single input (from one single source) without considering any uncertainty or variability and also use a very simplistic release model. However, they extend the flow modeling to additional materials not covered by Sun et al. [12]: SiO_2, Al-oxides, Fe and Fe-oxides, nanoclays, CeO_2, Cu, and CuO. To allow a comparison with the data from Sun et al. [12], the mass flows for the same four ENM are shown in Table 6, extrapolated to the EU.

9 Conclusions

This chapter has systematically evaluated what information is needed in order to quantify the flows of ENM to the environment and has reviewed the current state of knowledge. The life cycle thinking forms the basis of the evaluation. The first step in release assessment is the knowledge about the production and use of ENM. Data on production are crucial for the assessment, because they determine the maximal amount that could potentially be released. This starts with data on production amounts of ENM, where the main issue seems to be the definition what is actually an ENM and what is considered a conventional material. This is especially important for materials that have been on the market for decades, e.g., SiO_2, and are now, depending on the source [63], considered to be a nanomaterial or not. It can be expected that in the future data will be more comparable between different sources if the underlying definition that is used is the one proposed by the EU.

The different life cycles of products that are manufactured with the ENM are determining the release potential. The knowledge about the product distribution is therefore key to release estimation. This is needed in order to quantify the flows of ENM – the qualitative information that is available in many reviews, e.g., which potential applications exist, is only of limited relevance. Whereas product registers are helpful to some extent, it is much more important to get first-hand industry estimates about sectors and applications where the ENM are used. The current best way to go forward is to use probabilistic modeling as developed by [64] which is able to fully consider the uncertainty in model input values.

The two important life cycle steps that need to be considered are the use phase and the EoL treatment. During these steps experimental data from real-world release studies are the gold standard. However, in most cases release has been estimated or guessed based on standard knowledge about product use and behavior. In addition, release to the environment during production and manufacturing may occur. Information is lacking about real-world release studies that allow to quantify the transfer factors from product use to the receiving compartment. What is available are mostly lab-based studies that quantify the release of total chemical element under conditions mimicking more or less the release in real-world situations. A main issue is how the short-term data in laboratory experiments can be extrapolated to the whole life cycle of products. An example is that most washing experiments report percent silver released in one washing – how to extrapolate this to several years of washing at home? The transfer factors needed for material flow modeling integrate release over the whole lifetime of the product. The current models take the available short-term data and either apply a factor to derive full lifetime release or use the release data as is without any further adjustments. Release kinetics may be considerably different between the initial and later stages, and simple extrapolation may not be possible – both decreasing release overtime by rapid removal of weakly bound particles and an increase due to degradation of the matrix are possible.

The mass flows discussed in this report provide the input data to derive environmental concentrations [2]. In a simple approach, the ENM mass is mixed into environmental compartments of defined size in a regional assessment to derive PEC, and such values have been published [12, 60, 61]. The mass flows can also be adjusted to the local population to derive inputs into the environment in a local scenario. This approach has been used to calculate ENM concentrations in Swiss rivers with a high geographic resolution [65]. The mass flows to the environment will also be needed for environmental fate models that are based on mechanistic description of the reactions and the behavior of the released ENM in environmental compartments such as water or soils [66].

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References

1. EU (2011) Commission recommendation of 18 October 2011 on the definition of nanomaterial (2011/696/EU). Offi J L 275:38–40
2. Gottschalk F, Sun T, Nowack B (2013) Environmental concentrations of engineered nanomaterials: review of modeling and analytical studies. Environ Pollut 181:287–300
3. von der Kammer F, Ferguson PL, Holden PA, Masion A, Rogers KR, Klaine SJ et al (2012) Analysis of engineered nanomaterials in complex matrices (environment and biota): general considerations and conceptual case studies. Environ Toxicol Chem 31:32–49

4. Gottschalk F, Nowack B (2011) Release of engineered nanomaterials to the environment. J Environ Monit 13:1145–1155
5. Som C, Berges M, Chaudhry Q, Dusinska M, Fernandes TF, Olsen SI et al (2010) The importance of life cycle concepts for the development of safe nanoproducts. Toxicology 269:160–169
6. Schmid K, Riediker M (2008) Use of nanoparticles in Swiss industry: a targeted survey. Environ Sci Technol 42:2253–2260
7. Hendren CO, Mesnard X, Dröge J, Wiesner MR (2011) Estimating production data for five engineered nanomaterials as a basis for exposure assessment. Environ Sci Technol 45:2562–2569
8. Piccinno F, Gottschalk F, Seeger S, Nowack B (2012) Industrial production quantities and uses of ten engineered nanomaterials for Europe and the world. J Nanoparticle Res 14:1109
9. Keller A, McFerran S, Lazareva A, Suh S (2013) Global life cycle releases of engineered nanomaterials. J Nanoparticle Res 15:1–17
10. Future Markets (2012) The global market for nanomaterials 2002–2006: production volumes, revenues and end use markets. Future Markets Inc. http://www.futuremarketsinc.com/index.php?option=com_content&view=article&id=176&Itemid=73
11. ANSES (2013) Éléments issus des déclarations des substances à l'état nanoparticulaire. RAPPORT d'étude. ANSES (l'Agence nationale de sécurité sanitaire)
12. Sun TY, Gottschalk F, Hungerbühler K, Nowack B (2014) Comprehensive modeling of environmental emissions of engineered nanomaterials. Environ Pollut 185:69–76
13. Keller AA, Lazareva A (2013) Predicted releases of engineered nanomaterials: from global to regional to local. Environ Sci Technol Lett 1:65–70
14. Robichaud CO, Uyar AE, Darby MR, Zucker LG, Wiesner MR (2009) Estimates of upper bounds and trends in nano-TiO_2 production as a basis for exposure assessment. Environ Sci Technol 43:4227–4233
15. Project on Emerging Nanotechnologies (2008) An inventory of nanotechnology-based consumer products currently on the market http://www.nanotechproject.org/inventories/consumer/
16. Berube DM, Searson EM, Morton TS, Cummings CL (2010) Project on emerging nanotechnologies – consumer product inventory evaluated. Nanoetchnol Law Bus 7:152–163
17. Aitken RJ, Chaudhry MQ, Boxall ABA, Hull M (2006) Manufacture and use of nanomaterials: current status in the UK and global trends. Occup Med 56:300–306
18. Lo LY, Li Y, Yeung KW, Yuen CWM (2007) Indicating the development stage of nanotechnology in the textile and clothing industry. Int J Nanotechnol 4:667–679
19. Wijnhoven SWP, Dekkers S, Kool M, Jongeneel WP, De Jong WH (2010) Nanomaterials in consumer products. Update of products on the European market in 2010. RIVM Report 340370003/2010. http://www.rivm.nl/bibliotheek/rapporten/340370003.pdf
20. Nowack B, Brouwer C, Geertsma RE, Heugens EHW, Ross BL, Toufektsian M-C et al (2013) Analysis of the occupational, consumer and environmental exposure to engineered nanomaterials used in 10 technology sectors. Nanotoxicology 7(6):1152–1156
21. Nowack B, David RM, Fissan H, Morris H, Shatkin JA, Stintz M et al (2013) Potential release scenarios for carbon nanotubes used in composites. Environ Int 59:1–11
22. Geranio L, Heuberger M, Nowack B (2009) Behavior of silver nano-textiles during washing. Environ Sci Technol 43:8113–8118
23. Lorenz C, Windler L, Lehmann RP, Schuppler M, Von Goetz N, Hungerbühler K et al (2012) Characterization of silver release from commercially available functional (nano)textiles. Chemosphere 89:817–824
24. Windler L, Lorenz C, Von Goetz N, Hungerbuhler H, Amberg M, Heuberger M et al (2012) Release of titanium dioxide from textiles during washing. Environ Sci Technol 46:8181–8188
25. Lombi E, Donner E, Scheckel K, Sekine R, Lorenz C, von Götz N et al (2014) Silver speciation and release in commercial antimicrobial textiles as influenced by washing. Chemosphere 111:352–358

26. Farkas J, Peter H, Christian P, Urrea JAG, Hassellov M, Tuoriniemi J et al (2011) Characterization of the effluent from a nanosilver producing washing machine. Environ Int 37:1057–1062
27. Cleveland D, Long SE, Pennington PL, Cooper E, Fulton MH, Scott GI et al (2012) Pilot estuarine mesocosm study on the environmental fate of Silver nanomaterials leached from consumer products. Sci Total Environ 421:267–272
28. Kaegi R, Sinnet B, Zuleeg S, Hagendorfer H, Mueller E, Vonbank R et al (2010) Release of silver nanoparticles from outdoor facades. Environ Pollut 158:2900–2905
29. Al-Kattan A, Wichser A, Vonbank R, Brunner S, Ulrich A, Zuin S et al (2013) Release of TiO_2 from paints containing pigment-TiO_2 or nano-TiO_2 by weathering. Environ Sci Process Impacts 15:2186–2193
30. Al-Kattan A, Wichser A, Vonbank R, Brunner S, Ulrich A, Zuin S et al (2015) Characterization of materials released into water from paint containing nano-SiO_2. Chemosphere 119:1314–1321
31. Künniger T, Gerecke AC, Ulrich A, Huch A, Vonbank R, Heeb M et al (2014) Release and environmental impact of silver nanoparticles and conventional organic biocides from coated wooden façades. Environ Pollut 184:464–471
32. Hauri JF, Niece BK (2011) Leaching of silver from silver-impregnated food storage containers. J Chem Educ 88:1407–1409
33. Huang YM, Chen SX, Bing X, Gao CL, Wang T, Yuan B (2011) Nanosilver migrated into food-simulating solutions from commercially available food fresh containers. Packag Technol Sci 24:291–297
34. Song H, Li B, Lin QB, Wu HJ, Chen Y (2011) Migration of silver from nanosilver-ìpolyethylene composite packaging into food simulants. Food Addi Contam Part A 28:1758–1762
35. von Goetz N, Fabricius L, Glaus R, Weitbrecht V, Günther D, Hungerbühler K (2013) Migration of silver from commercial plastic food containers and implications for consumer exposure assessment. Food Addi Contam Part A 30:612–620
36. Harper S, Wohlleben W, Doa M, Nowack B, Clancy S, Canady R et al (2015) Measuring nanomaterial release from carbon nanotube composites: review of the state of the science. J Phys Conf Ser 617: 012026
37. Hirth S, Cena L, Cox G, Tomovic Z, Peters T, Wohlleben W (2013) Scenarios and methods that induce protruding or released CNTs after degradation of nanocomposite materials. J Nanoparticle Res 15:1504
38. Wohlleben W, Vilar G, Fernández-Rosas E, González-Gálvez D, Gabriel C, Hirth S et al (2014) A pilot interlaboratory comparison of protocols that simulate aging of nanocomposites and detect released fragments. Environ Chem 11:402–418
39. Quadros ME, Marr LC (2011) Silver nanoparticles and total aerosols emitted by nanotechnology-related consumer spray products. Environ Sci Technol 45:10713–10719
40. Lorenz C, Hagendorfer H, von Goetz N, Kaegi R, Gehrig R, Ulrich A et al (2011) Nanosized aerosols from consumer sprays: experimental analysis and exposure modeling for four commercial products. J Nanoparticle Res 13:3377–3391
41. Botta C, Labille J, Auffan M, Borschneck D, Miche H, Cabie M et al (2011) TiO_2-based nanoparticles released in water from commercialized sunscreens in a life-cycle perspective: structures and quantities. Environ Pollut 159:1543–1548
42. Gondikas AP, Kammer F, Reed RB, Wagner S, Ranville JF, Hofmann T (2014) Release of TiO_2 nanoparticles from sunscreens into surface waters: a one-year survey at the old Danube recreational lake. Environ Sci Technol 48:5415–5422
43. Holbrook DR, Motabar D, Quiñones O, Stanford B, Vanderford B, Moss D (2013) Titanium distribution in swimming pool water is dominated by dissolved species. Environ Pollut 181:68–74
44. Mueller NC, Buha J, Wang J, Ulrich A, Nowack B (2013) Modeling the flows of engineered nanomaterials during waste handling. Environ Sci Process Impacts 15:251–259

45. Froggett S, Clancy S, Boverhof D, Canady R (2014) A review and perspective of existing research on the release of nanomaterials from solid nanocomposites. Part Fibre Toxicol 11:17
46. Benn TM, Westerhoff P (2008) Nanoparticle silver released into water from commercially available sock fabrics. Environ Sci Technol 42:4133–4139
47. von Goetz N, Lorenz C, Windler L, Nowack B, Heuberger M, Hungerbuhler K (2013) Migration of Ag- and TiO_2-(nano)particles from textiles into artificial sweat under physical stress: experiments and exposure modeling. Environ Sci Technol 47:9979–9987
48. Nowack B (2014) Emissions from consumer products containing engineered nanomaterials over their lifecycle. In: Wohlleben W, Kuhlbusch TAJ, Lehr C-M, Schnekenburger J (eds) Safety of nanomaterials along their lifecycle: release, exposure and human hazards. Taylor & Francis, London. ISBN 978-1-46-656786-3
49. Bello D, Wardle BL, Yamamoto N, de Villoria RG, Garcia EJ, Hart AJ et al (2009) Exposure to nanoscale particles and fibers during machining of hybrid advanced composites containing carbon nanotubes. J Nanoparticle Res 11:231–249
50. Demou E, Stark W, Hellweg S (2009) Particle emission and exposure during nanoparticle synthesis in research laboratories. Ann Occup Hyg 53:829–838
51. Demou E, Peter P, Hellweg S (2008) Exposure to manufactured nanostructured particles in an industrial pilot plant. Ann Occup Hyg 52:695–706
52. Evans DE, Ku BK, Birch ME, Dunn KH (2010) Aerosol monitoring during carbon nanofiber production: mobile direct-reading sampling. Ann Occup Hyg 54:514–531
53. Huang C-H, Tai C-Y, Huang C-Y, Tsai C-J, Chen C-W, Chang C-P et al (2010) Measurements of respirable dust and nanoparticle concentrations in a titanium dioxide pigment production factory. J Environ Sci Health A 45:1227–1233
54. Lee JH, Kwon M, Ji JH, Kang CS, Ahn KH, Han JH et al (2011) Exposure assessment of workplaces manufacturing nanosized TiO_2 and silver. Inhal Toxicol 23:226–236
55. Hang J, Luo Z, Sandberg M, Gong J (2013) Natural ventilation assessment in typical open and semi-open urban environments under various wind directions. Build Environ 70:318–333
56. Kiwan A, Berg W, Fiedler M, Ammon C, Gläser M, Müller H-J et al (2013) Air exchange rate measurements in naturally ventilated dairy buildings using the tracer gas decay method with 85Kr, compared to CO_2 mass balance and discharge coefficient methods. Biosyst Eng 116:286–296
57. You Y, Niu C, Zhou J, Liu Y, Bai Z, Zhang J et al (2012) Measurement of air exchange rates in different indoor environments using continuous CO_2 sensors. J Environ Sci 24:657–664
58. Mitrano DM, Rimmele E, Wichser A, Erni R, Height M, Nowack B (2014) Presence of nanoparticles in wash water from conventional silver and nano-silver textiles. ACS Nano 8:7208–7219
59. Gottschalk F, Nowack B (2012) Modeling environmental release and exposure of engineered nanomaterials. In: Jerzy L, Tomasz P (eds) Towards efficient designing of safe nanomaterials. RSC, Cambridge
60. Mueller NC, Nowack B (2008) Exposure modeling of engineered nanoparticles in the environment. Environ Sci Technol 42:4447–4453
61. Gottschalk F, Sonderer T, Scholz RW, Nowack B (2009) Modeled environmental concentrations of engineered nanomaterials (TiO_2, ZnO, Ag, CNT, fullerenes) for different regions. Environ Sci Technol 43:9216–9222
62. ECHA (2010) Guidance on information requirements and chemical safety assessment Chapter R.16: Environmental Exposure Estimation, European Chemicals Agency
63. Bosch A, Maier M, Morfeld P (2012) Nanosilica? Clarifications are necessary! Nanotoxicology 6:611–613
64. Gottschalk F, Scholz RW, Nowack B (2010) Probabilistic material flow modeling for assessing the environmental exposure to compounds: methodology and an application to engineered nano-TiO_2 particles. Environ Model Softw 25:320–332

65. Gottschalk F, Ort C, Scholz RW, Nowack B (2011) Engineered nanomaterials in rivers – exposure scenarios for Switzerland at high spatial and temporal resolution. Environ Pollut 159:3439–3445
66. Praetorius A, Scheringer M, Hungerbuhler K (2012) Development of environmental fate models for engineered nanoparticles – a case study of TiO_2 nanoparticles in the Rhine river. Environ Sci Technol 46:6705–6713

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