



nanoMONITOR



Guidance on the sampling methods and analytical techniques for the measurement and monitoring of engineered nanomaterials in the environment



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DISCLAIMER

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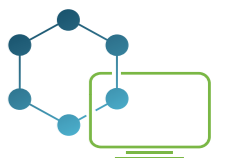
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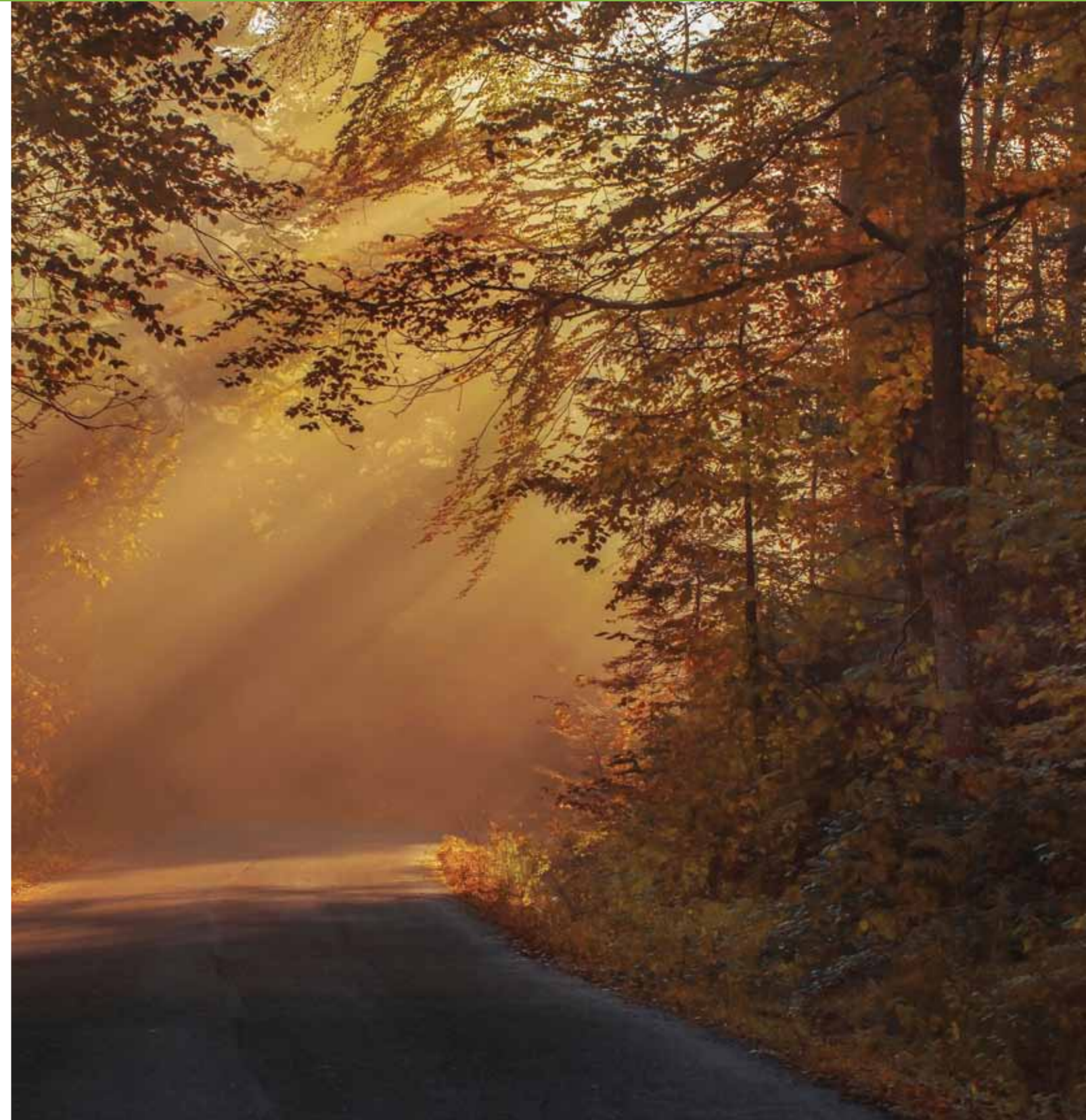


EXECUTIVE SUMMARY

This guidance has been produced as part of the scheduled activities of the LIFE project NanoMONITOR, focused on the development of an integrated approach to overcome current data gaps on the concentration of engineered nanomaterials (ENMs) in indoor workplaces and urban areas by combining long series of robust data measures by a new wireless sensor network of monitoring stations and a tailored designed data management application.

ENMs are known to exhibit unique characteristics that distinguish their behaviour from bulk materials, including much larger specific surface area and surface activity (Hsieh et al., 2013) or much larger deposition rate in the respiratory systems (Silva et al., 2013), which may lead to unanticipated effects to human health, including pro-inflammatory effects and possible development of fibrosis and /or cancer (Shi et al., 2013), as well as to significantly alter ecosystems and cause adverse effects on the metabolism of living beings (Sauvé, 2014).

NanoMONITOR tackles the challenge of contributing to a proper understanding of the concentration levels and nature of the ENMs in urban air, considering that these types of emerging pollutants are known to enter urban areas through accidental spills or during the use and disposal of nanotechnology products (Kumar et al., 2014b; Lowry et al., 2012; Stone et al., 2010).



1. SCOPE AND GOALS

1.1 Purpose of the Guidance

The *Guidance on the sampling methods and analytical techniques for the measurement and monitoring of engineered nanomaterials (ENMs) in the environment* provides support to select adequate sampling and monitoring procedures and techniques to characterise the concentration of ENMs in heterogeneous environments, including industrial settings, indoor and outdoor areas in urban locations and natural environments. The guidance also aims at making current data relative to the potential sources and concentration of ENMs in indoor workplaces and urban areas accessible and interoperable.

The ultimate goal of this document is to provide guidance for indoor, outdoor and personal exposure monitoring of particles in the nanometer range, as well as data management to ensure that measured data are correct, representative and consistent.

By developing a real-time information and monitoring system NanoMONITOR supports the generation of new knowledge on the concentration of ENMs – a key aspect to provide insights into the environmental, health, and safety implications of ENMs

1.2 Scope of the Guidance

This document provides best-practices for undertaking sampling and monitoring activities in indoor workplaces, urban areas and relevant environmental compartments, which include surface water, ground water, wastewater, sediments, and soils. In detail, the guidance includes:

- 1. Sampling and monitoring techniques to detect, analyse and quantify ENMs in heterogeneous environments**
This guidance includes recommended procedures to detect, analyse and quantify ENMs in heterogeneous environments, ranging from urban areas to surface water. A compendium of operative procedures to support the sampling, monitoring and analysis of the concentration of ENMs in industrial settings, subway systems, high traffic areas, as well as heterogeneous ecosystems such as surface water, ground water, wastewater, sediments, and soils were developed and are summarised in this guidance.
- 2. Supporting information on the use measured data for regulatory risk assessment**
This guidance provides insights into the minimum set of meta-data needed to use measured data on the concentration of ENMs under the EC regulation REACH. These include: contextual information of the scenario measured; specifications of the sampling techniques and measurement devices used; properties of the ENMs reported; and others.
- 3. Data on the concentration of ENMs in urban areas, including subway systems and high traffic areas**
Current data on the concentration of ENMs in urban areas is still scarce mainly due to the lack of instrumentation to distinguish ENMs from background ultrafine particles. This guidance compiles data generated in the course of the project, providing new information on the expected concentration of ENMs in urban areas.

1.3 Target Audience

The guide is primarily intended to be used by health and safety advisors, researchers and policy makers. It should be noted that the recommendations included in this guideline do not imply that they are endorsed or recommended by international organisations and/or regulatory bodies. The responsibility for the interpretation and use of the material lies with the reader.

The guidelines are targeted specifically at:

- Health and safety advisors who are responsible for the health and safety of workers exposed to ENMs
- Experts from industry associations and other stakeholder organisations informing companies about the requirements for the risk assessment of ENMs on a regulatory basis, especially in industrial settings
- Experts from standardisation (i.e. ISO committees) and/or regulatory bodies (i.e. ECHA)
- Policymakers at the local, national or international level, who are responsible for the health and safety of workers exposed to manufactured nanomaterials (MNMs)
- Policymakers at the local, national or international level, who are responsible for the definition of emerging pollutants in air quality programmes.

1.4 Structure

The members of the consortium defined the structure of the guidance, covering those aspects considered of special relevance to support stakeholders in the identification of the levels of exposure to ENMs by target populations, including workers dealing with the production and use of ENMs, as well as citizens that might be exposed due to the unintentional release of ENMs into the environment. The guidance contains the following sections:

CHAPTER 1. (This chapter) describes the aims of the document and sets its scope

CHAPTER 2. Introduction.

- Environmental, health, and safety implications of ENMs
- Exposure assessment and monitoring under REACH

CHAPTER 3. Analysis of current knowledge on the concentration levels of ENMs in indoor workplaces and the environment

- Type and sources of ENMs in workplaces and the environment
- Levels of exposure in workplaces
- Environmental levels of ENMs in the environment

CHAPTER 4. Recommendations for the exposure assessment of ENMs in the workplace

- Recommended measurement techniques and protocols
- Data management and reporting

CHAPTER 5. Recommendations for the exposure assessment of ENMs in the environment

- Recommended measurement techniques and protocols for detecting, quantifying, and characterising of ENMs in surface water, ground water, and wastewater
- Recommended measurement techniques and protocols for detecting, quantifying, and characterising of ENMs in sediments and soils
- Recommended measurement techniques and protocols for detecting, quantifying, and characterising airborne ENMs in urban areas
- Data management and reporting

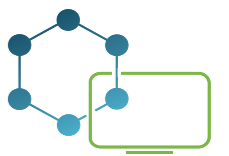
CHAPTER 6. Regulatory challenges

Further guidance documents will be published on the project website when they are finalised or updated.

This guideline provides risk assessors and stakeholders with an overall view of available data on the concentration of ENMs in relevant areas, as well as a set of standard operating procedures to ensure the quality and comparability of the data published.

Additional information of specific topics of the guidance and/or details on project outcomes can be requested directly contacting the project coordinator:

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2. INTRODUCTION

2.1 Environmental, health, and safety implications of engineered nanomaterials

Advancements in the fields of nanoscience and nanotechnology have resulted in myriad possibilities for industrial and consumer product applications (Vance et al., 2015), facilitating major breakthroughs in different application domains. However, the nanoscale opens the doors to new or different potential risks on human health and the environment that are still not fully explored.

The unique properties of engineered nanomaterials (ENMs), including much larger specific surface area and surface activity, may result in **health and environmental hazards different from those demonstrated by same materials in bulk form**. Of particular importance is their small size, which may allow for increased penetration of environmental and biological barriers. In addition, ENMs have much larger surface areas than similar masses of large scale materials. A larger surface area provides a larger interface for molecular and chemical interactions within the external environment, potentially promoting their reactivity.

The evaluation of the potential impact of ENMs on human health and the environment requires data on both effects and exposure. In this sense, current knowledge on the **potential hazards posed by ENMs** on human health and the environments comes from in vitro studies conducted in organ-specific cell lines, including human epidermal cells, human dermal fibroblasts, human embryo kidney cells and human bronchial cells, as well ecotoxicological studies conducted in model organisms at different trophic levels such as bacteria, algae, and fish.

Such studies show several adverse effects for both human health and biota, including cellular toxicity (Sayes et al., 2005) and DNA damage (Lindberg et al., 2009) in human cell lines, and cellular level toxicity for both unicellular and higher organisms, including organelle dysfunction and DNA damage.

In terms of **exposure potential**, the vast majority of studies are focused on workplace areas, where inhalation is the most common route of exposure. Although skin has also been investigated, most studies have shown little to no transdermal ENMs absorption (Karjalainen et al., 2012). In terms of environmental exposure, there is a scientific agreement that ENM production, use and disposal lead to environmental release of ENMs (Gottschalk and Nowack, 2011). However, very little is known on emissions of ENMs to the environment.

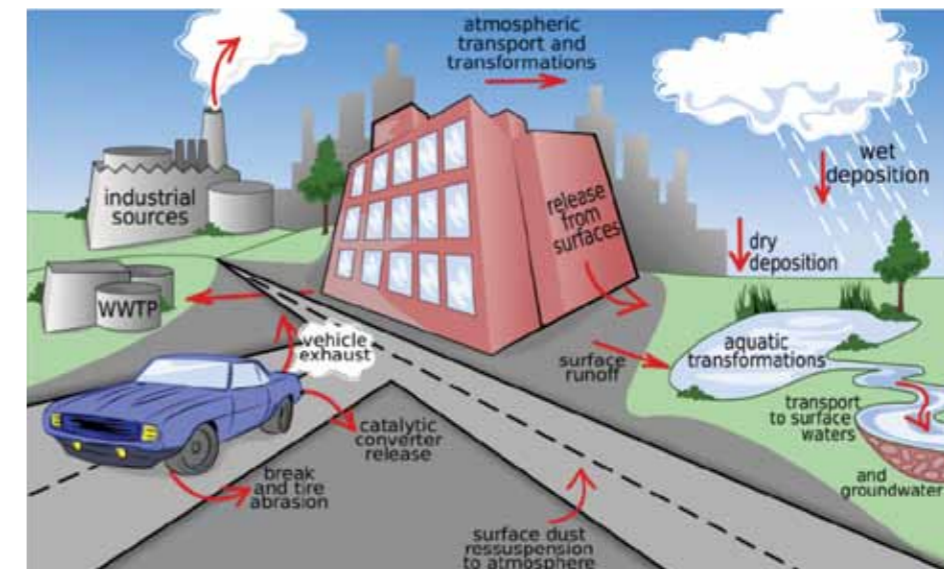
In contrast to occupational exposure, **current studies focused on the environmental release** of ENMs and exposure to ENMs in areas other than industrial settings (e.g. urban areas) **are scarce**, which is mainly due to the lack of techniques to quantitatively monitor ENM emissions and concentrations in urban areas and/or the environment, and hence, very little is known about the presence, type, composition and form of released ENMs.

It has to be noted that any evaluation of the exposure potential to ENMs has to consider a wide range of emissions sources, especially in the case of urban areas and the environment, where a wide number of sources exist, ranging from **indirect releases** (e.g. air exhaust or wastewater) during the production of ENMs in industrial settings to **intended or unintended releases** of ENMs during the use phase of products containing ENMs, including textiles, paints, sunscreens, food additives or plastic based products among other nano-enabled products.

The main route of entry into the environment is due to indirect emissions of ENMs from industrial settings, as well as uncontrollable releases into the environment during the use, recycling and disposal of nano-enabled products. In this regard, accidental spills during production or later transport of nanomaterials, and release from wear and tear of materials containing ENMs may lead to potential exposure (Lützhøft et al., 2015). Similarly, wastewater treatment streams, landfill leachates and waste incineration products are all likely to contain nanomaterials from nano-enabled products disposed of at the end of their useful life.

In addition, incidental nanomaterials (INMs) can also be generated in outdoor urban environments by automobiles, power plants and urban based industries (Buseck and Adachi, 2008; Kumar et al., 2014). Figure 1 shows a list of potential sources of release and routes of entry of ENMs and INMs in urban environments highlighting INMs produced unintentionally by engines and/or break and tire abrasion, and ENMs produced in industrial areas but transported to urban areas.

Figure 1: Sources and pathways of outdoor urban nanomaterials in the environment (Baalousha, et al., 2016)



Besides outdoor environments, existing evidence suggest that subway systems may be also of interest, including elevated levels of fine (PM_{2.5}) and coarse (PM_{2.5-10}) particulate air pollution, as well as ultrafine particles (UFP), understood as particles smaller than 100 nm, with a chemical composition based on elements such as Fe, Mn, Si, Cr, Cu, Ba, Ca, Zn, Ni and K.

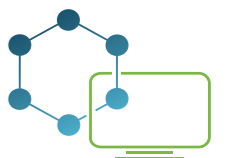
Both INMs and the smallest fractions of ambient particulate matter (ultrafine fraction) posse unique properties, many of which are not shown by their bulk equivalents (Yang et al., 2017), being also of potential concern to human health considering that these nanoscale particles can penetrate the lung's alveolar (air-sack) membranes and thereafter translocate into the bloodstream to other organs.

Studies conducted over the last decade reported **direct correlation with adverse effects**, especially cardiopulmonary diseases (e.g., asthma, chronic obstructive pulmonary disease, arrhythmia, heart attack). Moreover, neurological consequences have been showed in experimental animal models, but little is known in humans.

Finally, in terms of data availability, current data on the concentration of ENMs in the environment is very limited as a result of the lack of techniques capable of collecting, preserving and storing samples containing ENMs (Lin et al., 2010), as well as of the little understanding of the ENMs properties and their behaviour in the environment.

Current data are mainly drawn from modelling studies based on mathematical approaches used to deal with the high uncertainty on the release rates and distribution of ENMs in the environment. Nevertheless, average exposure concentrations are expected to be in the parts per billion (ppb) range.

The evaluation of the potential effects of ENMs on ecosystems is already a challenge, with a limited number of ENMs evaluated at various biological levels using high throughput screening (HTS) with cells and embryos, bioassays with aquatic and terrestrial organisms, and studies with microorganisms.



2. INTRODUCTION

2.2 Exposure assessment and monitoring under REACH

As any chemical, ENMs are covered by the EC regulation 1907/2016 on the Registration, Evaluation, Authorization and Restriction of Chemical substances (REACH), and the EC regulation 1272/2008 on the classification, labelling and packaging of substances and mixtures (CLP Regulation).

The REACH regulation aims to improve the protection of human health and the environment through the better identification and evaluation of the potential risks posed by chemicals. Under REACH, risk assessment and risk characterisation are conducted under the overall framework of the chemical safety assessment (CSA) process, by which a registrant shall identify and describe the conditions under which the manufacturing and use of a substance is considered to be safe during each life cycle step.

In the light of current knowledge and opinions of the EU Scientific and Advisory Committees and independent risk assessors, current risk assessment methods are applicable, even if work on particular aspects of risk assessment is still required due to the current lack of standardised approaches for determining the hazards and levels of exposure to the human health and the environment. In this regard, it has been acknowledged (e.g. by the OECD chemicals programme on cooperation on risk assessment) that the existing risk assessment paradigm developed for traditional chemicals should also be applied to ENMs (OECD, 2012). Nevertheless, these steps need specific considerations in practice when applied to ENMs (e.g. metric to use, exposure assessment methodology, etc.).

In a situation when several nanomaterials have already entered the market, a comprehensive risk assessment of ENMs is needed, including information with respect to the intrinsic properties of the particle that may assist in identifying the presence or absence of hazardous properties, as well as the likelihood of exposure in a specific compartment (i.e. workplace, consumers and the environment).

In this context, and considering the scope and goals of the NanoMONITOR project, a better knowledge on the concentration of ENMs at workplaces, urban areas and the environment are of special relevance to support the risk assessment process under REACH. A list of REACH information requirements can be completed or complemented with chemical monitoring data "measured data", including data on the concentrations of ENMs in the workplace or in effluents, for example waste-water streams.

For use in REACH, standards are high and registrants relying on monitoring data in the registration dossiers must ensure that measured data are representative, repeatable and well documented, including information on the sampling and analytical methods used.

A detailed vision of the main REACH requirements where measured data is applicable are depicted in Table 1, highlighting: 1) use of measured data to support exposure estimations, 2) use of measured data to show adequateness of risk management measures (RMMs), 3) in-house exposure assessment (enforcement), and 4) self-monitoring of emissions (enforcements).

In terms of human health, the use of measured data to support the identification of safe exposure scenarios is of prime importance when dealing with ENMs. Exposure scenarios are sets of information describing the conditions under which the risks associated with the identified use(s) of a substance can be controlled.

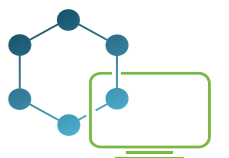
For each defined exposure scenario, the potential exposure is calculated considering the conditions of use and RMMs implemented. In this regard, REACH requires that existing adequately measured, representative exposure data are taken into account in the exposure assessment, either on their own or in combination with modelled exposure estimates. However, current Tier 1 exposure estimation models are not directly applicable to ENMs, and robust data on the performance levels of current RMMs is still scarce.

Table 1. Use of measured data under REACH provisions

PROCEDURE	ADDED VALUE	DOCUMENTATION	ACTOR
Registration	Release and exposure estimations	Chemical Safety Report Safety Data Sheets	M / I
	Persistence and bioaccumulation assessment	Chemical Safety Report	M / I
	Local and regional exposure estimation and predicted environmental concentrations (PECs)	Chemical Safety Report	M / I
Supply chain communication	Use of monitoring data to show adequateness of risk management measures	In house procedures	DU
	Use of monitoring data to prove local accumulation / effects of substances	Extended Safety data sheets (eSDS)	
Authorisation	Information on persistency, bioaccumulation, background concentrations and timelines as criteria for inclusion into Annex XIV.	Authorisation application	MS ECHA
	Voluntary monitoring programmes as argument for non-prioritization of substances for inclusion in Annex XIV		M I DU
	Application for an authorization (based on registration dossier of substance)		
Success-control and enforcement	Control of company-specific risk management measures: individual companies can use monitoring data on a local scale to control the effectiveness of implemented risk management measures and operational conditions.	In house procedures Extended Safety data sheets (eSDS)	M I DU

List of abbreviations: MS: Member State; M: manufacturer; I: Importer; DU: Downstream user;

Source: Environmental Research of the Federal Ministry for the Environment, Nature Conservation and Nuclear Safety. Report Number UBA-FB 00. 2013



2. INTRODUCTION

The use of measured data when dealing with ENMs will be always preferred. However, when measured data sets are used, there should be sufficient contextual information available to derive exposure scenarios (describing the conditions of use leading to exposure measured including any controls that are in operation). Potential sources of measured data which could be used are:

- Measured data taken under the actual exposure settings for the exposure scenario to be developed (company data). For example, data generated to comply with other legislation or to evaluate the effectiveness of the RMMs in place. Measured data required for site licenses and permits (with documented number/frequency of sampling, analytical methods, basic statistics) can be a good source of information for REACH
- Exposure information from monitoring databases with regulatory purposes, when information requirements enabling a robust assessment are fulfilled
- Exposure information from peer reviewed publications, when information requirements enabling a robust assessment are fulfilled
- Biomonitoring data
- Simulated process data.

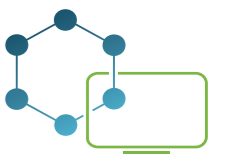
In terms of environmental risk assessment, according to the ECHA Guidance on Information Requirements and Chemical Safety Assessment. Chapter R.16: Environmental exposure assessment, actual measured concentrations of the substance in a particular environmental compartment can be used to refine modelled predicted environmental concentrations (PECs) and when appropriate, directly as PEC values. It should be noted that measured data at the local scale are representative of specific situation, being clearly linked to the operational conditions and risk management measures described in the exposure scenario.

When PECs have been derived from both measured data and calculation, they need to be compared. If they are not of the same order of magnitude, analysis and critical discussion of divergences are important steps for developing an environmental risk assessment of substances.

When measured data sheets are used, such data must be of a suitable quality, supported by sufficient contextual information, and be assigned to an appropriate spatial scale (local or regional).

In all cases, information to satisfactorily support the suitability and representativeness of the data is needed. Indicators of good quality include:

- reference to: quality schemes, standard sampling, and measurement methodologies
- context: enough description to support the intended scope
- clear description of monitored tasks
- clear information on risk management measures in operation during sampling
- details of duration and frequency of tasks and an assessment if the sampling duration is representative of full-shift exposure or only for the task duration
- whether data are current rather than historical (i.e. sampling period to be reported)
- collection from a wide range of the sites and processes covered by the use description
- statistical descriptors available.



3. ANALYSIS OF CURRENT KNOWLEDGE ON THE CONCENTRATION LEVELS OF ENMS IN INDOOR WORKPLACES AND THE ENVIRONMENT

3.1 Sources and forms of ENMs in target compartments

Airborne nanosized particles can originate from naturally occurring and incidental sources in addition to the engineered particles (ENPs) sources typically of interest in occupational settings. A highest exposure potential exists for workers in workplaces, where these materials are produced, used, or handled (Asbach, 2015).

The information on the concentration levels of ENMs in urban areas and/or ecosystems is still scarce, with a limited number of studies available. However, the number of published data on the levels of exposure to engineered nanomaterials (ENMs) in the workplace has increased substantially over the last five years, including data on the particle number concentration (particles/cm³) and mass concentrations (µg/cm³) measured using real-time measurement devices.

The sources of ENMs in workplaces are related with the type of processes and work practices conducted in the industrial facilities. Schneider et al., 2017 proposed a classification based on the definition of four source domains (Table 2) based on the life cycle stages, from production, downstream use, to end-of-life treatments.

The form and amount of the ENMs released in workplaces are determined by the activity emission potential and the substance emission potential. The activity emission potential is commonly related with the number of products (i.e. ENPs or nanoproducts) used, energy applied in the process and level of containment. Common forms of ENMs releases in workplaces include single particles and aggregates < 1000 nm, large agglomerates with a size range from 1 to 20 µm, as well as ENMs embedded into a solid matrix.

The substance emission potential can be considered specific of each ENM or nanoproduct. For ENMs in powder form, the emission potential will be determined by the dustiness of the material. In the case of colloidal dispersions containing ENMs, the concentration of the solute, diameter of dispersed ENMs, and the viscosity of the mixture are key parameters influencing the emission potential.

Concerning **urban areas**, the study of the magnitude of the exposure to ENMs in cities is already a challenge. The main sources of release include **unintentional emission** from nano-enabled products used in urban building and other infrastructures, and **industrial emission** that can reach the urban areas due to complex transport process in the atmosphere.

Table 2. Examples of emission sources

EMISSION SOURCE	RELEASE POTENTIAL	SPECIFICATIONS
1. Point source or fugitive emissions		
Liquid-phase reaction	Likely	Single particles
Flame spraying	Likely	Single particles
CVD	Not Excluded	Single particles
Top-down (milling)	Not excluded	Single particles
2. Handling and transfer of bulk manufactured nanomaterial powders with relatively low energy		
Weighing of powders	Likely	Single particles and aggregates < 1000nm
Harvesting	Likely	
Manual packaging (Bagging)	Likely	
Bag emptying of powders	Likely	Single particles and aggregates < 1000nm Large aggregates 1 to 20µm
Melt Blending	Likely	Embedded particles. Limited release of fully dissociated NPs
3. Dispersion of either (liquid) intermediates containing highly concentrated (> 25%) nanoparticles or application of (relatively low concentrated < 5%) ready-to-use products		
Spraying of liquid	Very Likely	Single aggregates as well as large agglomerates
Spraying (gas)	Very Likely	
Injection Moulding	Very Likely	Single particles and aggregates < 1000nm
Brushing and rolling	Very Likely	Embedded particles Limited release of fully dissociated NPs
Sonication of nanodispersions	Very Likely	Single particles and aggregates < 1000nm
4. Activities resulting in fracturing and abrasion of manufactured nanoparticles-enabled end-products		
Abrasion of nanoproducts	Not excluded	Embedded particles. Limited release of fully dissociated NPs

At present, there are **few studies on revealing the concentration of ENMs in urban areas**, however, ENMs are currently widely incorporated in new applications and products such as building façade paintings, fuel additives, photocatalytic concrete pavements or antireflection layers for road signs and pane, which means that a bigger number of ENMs that are likely to be released in the indoor and outdoor urban environments.

The effect of wind and rain, as well other weather conditions trigger ENMs erosion that can lead to air/water transport and deposition, which implies a potential exposure to ENMs of citizens. In addition, as indicated in the previous chapter, incidental nanomaterials (INMs) can also be generated in the outdoor urban environment by automobiles, power plants and urban based industries. In this regard, INMs can be released due to road traffic via engine combustion exhaust, brake pad and tire abrasion, with average particle diameter below 300 nm (Kumar et al., 2014), and compositions ranging from metals and metal oxides to phosphates. These INM contribute to a negligible portion of the total mass of particulate matter (PM), but they are the dominant fraction in terms of particle number (Kukutschová et al., 2011).

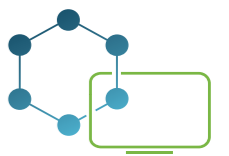
Rail traffic is also a potential source of INMs, being mainly generated by the motion of trains movements and activities of commuters and subway staff, air ventilation and various stationary processes (Martins et al., 2015). Evidence suggests that although abrasive forces between wheels, rail, and brakes can generate coarse and fine particles due to sharing, ultrafine particles can be generated via the high temperature of friction at interfaces between these components, with subsequent vaporisation of the substrate (Sundh et al., 2009).

As an example, the levels of ultrafine particles measured with a condensation particle counter (CPC, TSI model 3007) reached an average value of 14.200 pt/cm³ for the metro systems of Toronto, Montreal, and Vancouver, in Canada (Van Ryswyk et al., 2017). In the subways system of Helsinki, UPF concentration reached levels rather similar to those in outdoor ambient air (31.000 pt/cm³).

A non-exhaustive list of the sources and types of ENMs in urban system is depicted in Table 3.

Table 3. Examples of emission sources and types of ENMs in urban areas

SOURCE	EMISSION TYPE	MAIN USES OF ENMs
Nano-enabled products	Unintended releases during use	Metal and Metal Oxides (Ag, Cu, TiO ₂ , ZnO, SiO ₂ , CuO)
		Carbonaceous materials (Graphene) ENM particles heteroaggregated with background aerosols
Industrial emissions (Wet/dry atmospheric deposition in cities)	Direct release and transportation	Metal and Metal Oxides (Ag, Cu, TiO ₂ , ZnO, SiO ₂ , CuO)
Industrial emissions	Direct release and transportation	ENM particles heteroaggregated with background aerosols
Road Traffic		
Brakes/tires abrasion	Direct releases of Incidental Nanomaterials (INMs)	SiO ₂ , CeO ₂ , Zn, Mn, Fe, Co, Ni, Cd and Pb
Engine combustion exhaust		
Resuspension		
Rail Traffic		
Brakes/tires abrasion	Direct releases of Incidental Nanomaterials (INMs)	CuO Al, Ba, Ca, Cl, Cr, Cu, Fe, K, Mg, Mn, I, Pb, S, Si, Ti and Zn
Resuspension		



3. ANALYSIS OF CURRENT KNOWLEDGE ON THE CONCENTRATION LEVELS OF ENMS IN INDOOR WORKPLACES AND THE ENVIRONMENT

Finally, there are still insufficient qualitative and quantitative data on the concentration of ENMs in air, soil or water ecosystems. Very few studies have been conducted so far and possible existing forms and proportion of ENMs in the environment remain unclear mainly due to methodological challenges to detect and measure ENMs in complex systems, as well as current uncertainties on the fate and behaviour of ENM in ecosystems, both processes affected by the properties of the particles (e.g. size, geometry, surface properties), and the properties of the surrounding environmental medium (e.g. pH value, salinity, concentrations of naturally occurring organic substances).

Sanchis et al (2011) presented the first atmospheric study on the concentrations of fullerenes reporting median aerosol phase concentrations for C60 and C70 fullerenes of 0.06 ng/m³ and 0.48 ng/m³ respectively. A recent study conducted by Khosravi et al in 2012 presented ICP-MS data on Ti in wastewaters and sewage sludges, providing measured concentrations of 1.8 ng/ml and 317.4 ng/mg for the wastewater samples and biosolids respectively. An example of the main emission sources and expected types of ENMs in the environment are depicted in Table 4.

The form in which ENMs can be found in indoor workplaces, urban areas or the environment is affected by a number of variables, including the surface chemistry of the ENM, chemical properties of the media, or contents in organic matter among others.

As can be derived from the previous tables that primary particles are normally expected in industrial facilities, where ENMs are produced, used, or handled. In ecosystems, especially in water, these particles aggregate to form much larger particles, showing little propensity to disaggregate over periods of several months or more. A simplified vision of the expected types of ENMs for each compartment is depicted in Figure 2.

The air compartment is of prime importance under NanoMONITOR. As commented previously, so far most published studies focused on assessing workers' exposure whilst there had been very little studies tackling the release of ENMs into the environmental air compartment.

Current literature agrees that the main point sources at production plants are emissions from stacks which either stem from process flows from reactors and process units, or ventilation flows from working areas or specific working steps. Table 5 shows an overall view of the main sources of release of ENMs to the air compartment in industrial facilities.

Based on expert judgement, the amount of ENMs released in the environment from production sites range from 0.7 % to 1.6 % of which 6% is estimated to be emitted through air (Support for 3rd regulatory review on nanomaterials, 2016).

The 3rd regulatory review on nanomaterials includes a qualitative inventory of a subset of 12 ENMs selected in view of current hazard information and amount used. The preliminary release in the air compartment is depicted in Figure 3.

Figure 2. Schematic vision of the expected forms of ENMs in targeted compartments

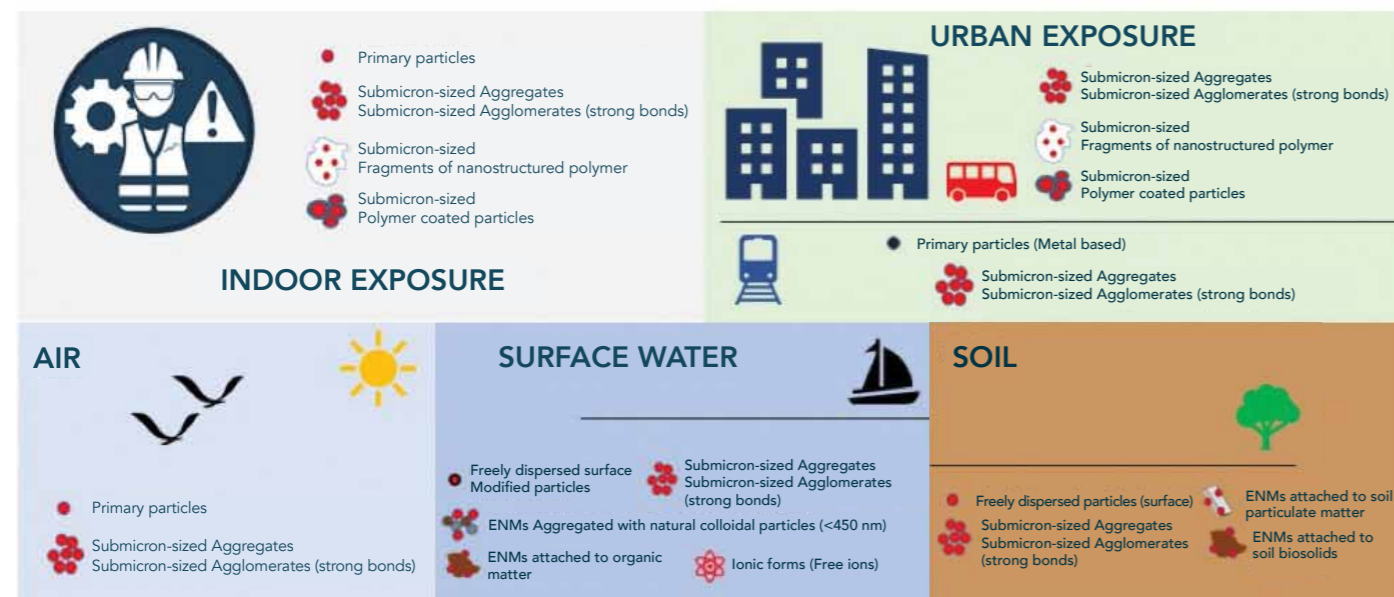


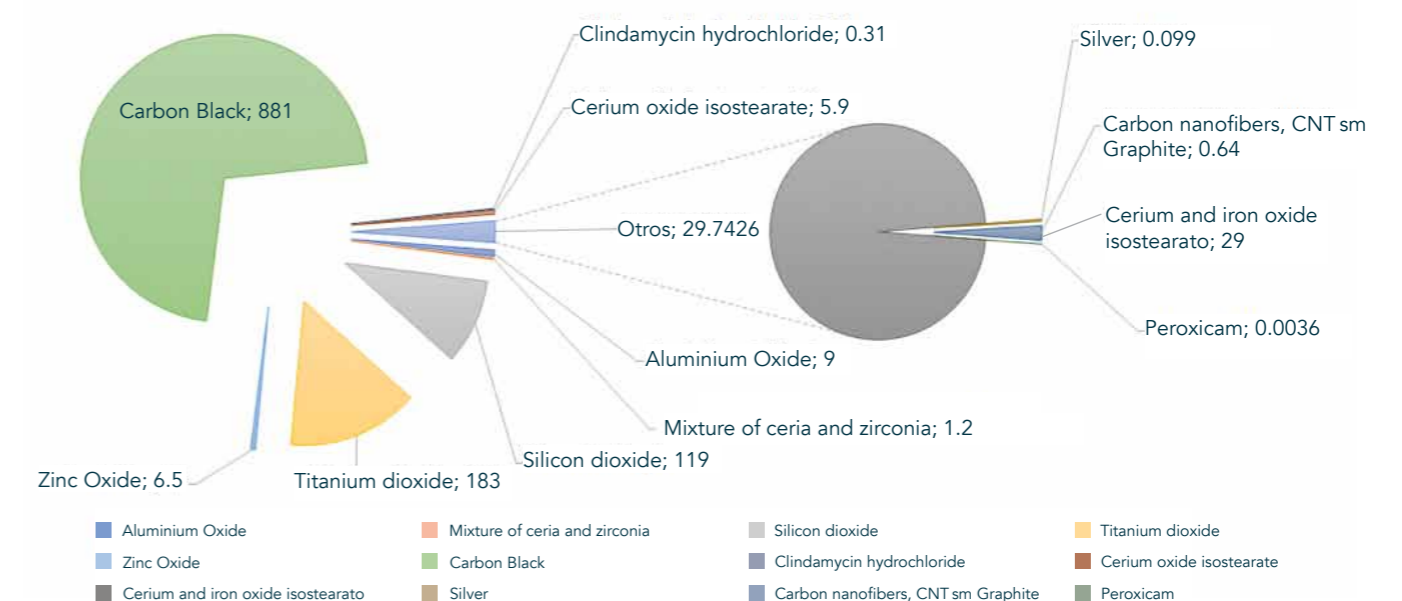
Table 4. Examples of emission sources and types of ENMs in environmental compartments

SOURCE	COMPARTMENT	MAIN TYPES OF ENMs
Direct release	Air (Atmosphere)	Freely dispersed Single particles and aggregates < 1000nm
Indirect release (resuspension / coastal splash)	Air (Atmosphere)	Single particles and aggregates < 1000nm
Indirect release (incineration plants)	Air (Atmosphere)	Single particles and aggregates < 1000nm
Direct release (application of ENMs in soil remediation)	Soil	Freely dispersed Single particles and aggregates < 1000nm
Indirect release (runoff)	Soil	
Indirect release (landfills)	Soil	
Unintended release (accidental spill)	Soil	
Dry/Wet deposition of airborne ENMs	Freshwater / Marine Soil	Single particles and aggregates < 1000nm
Direct release (via treated wastewater effluent)	Waste water	Aggregates <1000nm (Homo and heteroaggregates)
Unintended release (accidental spill)	Freshwater / Marine	ENMs heteroaggregated with natural colloidal particles (> 450nm)

Table 5. Sources of release of ENMs to the air compartment

SOURCE	COMPARTMENT
Stacks	Reactors
	Ventilation flows from Process units
Accidental emissions	Handling and transport operations
	Loss of containment
	Fire and explosions
Diffuse emissions	Storage, handling and transport of ENMs and nano-enabled products
	Cleaning operations
	Resuspension of ENMs deposited on the ground by accident
End of life treatments	Landfill disposal
	Incineration

Figure 3. Estimated release of ENMs of special interest to the air compartment (Tons)



3. ANALYSIS OF CURRENT KNOWLEDGE ON THE CONCENTRATION LEVELS OF ENMS IN INDOOR WORKPLACES AND THE ENVIRONMENT

3.2 Levels of exposure in workplaces

As stated previously, the highest exposure potential exists for workers at industrial facilities, where these materials are produced, used, or handled. Different activities where a potential risk of workers' exposure to ENMs may occur extends from discovery to disposal, including production, downstream use, maintenance or end-of-life processes.

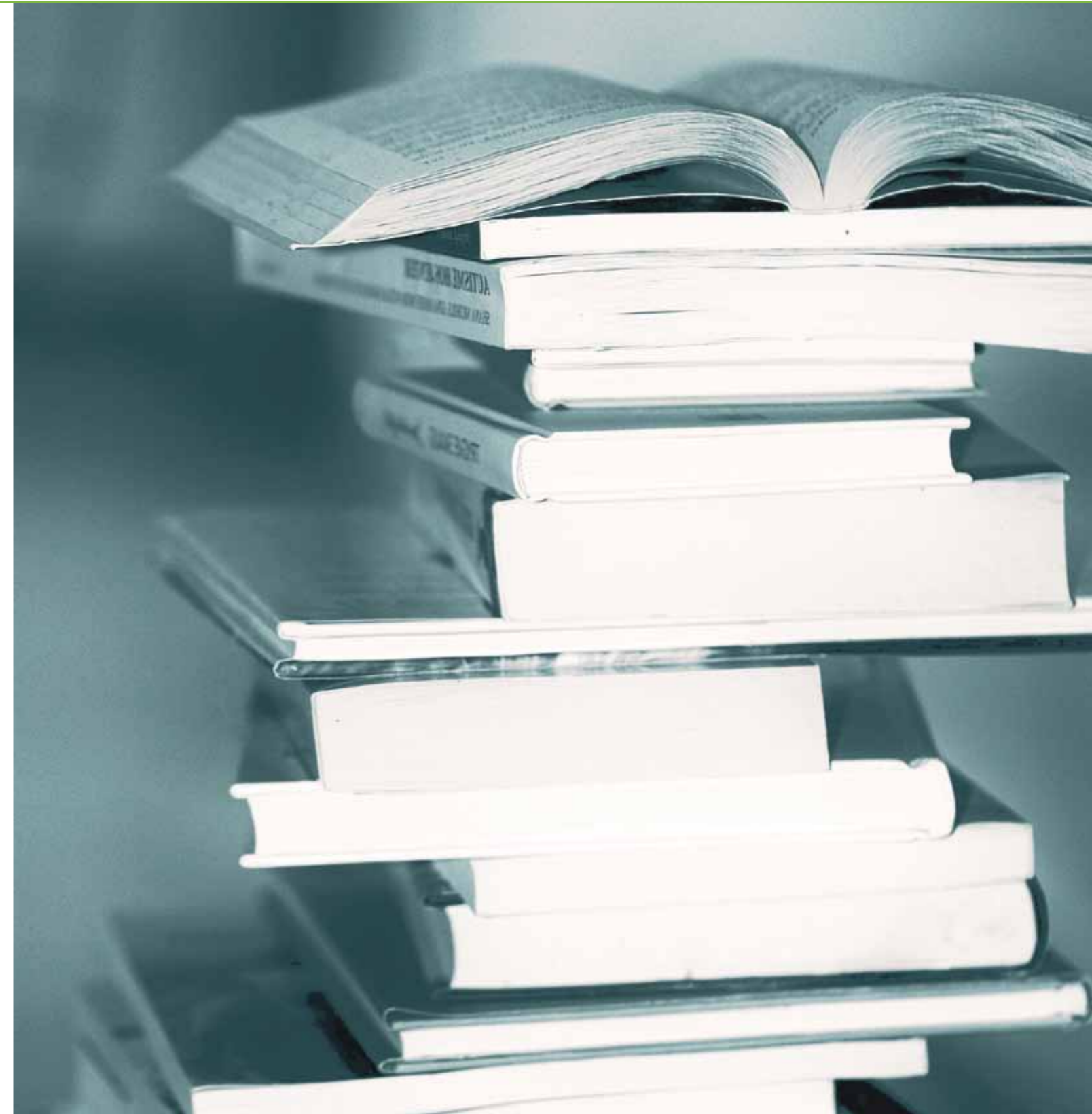
A proper definition of the potential situations of exposure to engineered nanomaterials constitutes a critical step for exposure assessment. Some examples of common exposure situations and measured concentrations in terms of particles number concentration (particles/cm³) are depicted in Table 6.

As it can be derived from the table, common activities at industrial facilities include weighing, mixing, sieving, bagging, or cleaning. The data on the levels of exposure measured using direct reading portable instruments, including particle counters (CPC/Nanotracer/DISCmini), and high-resolution devices such as the Scanning Mobility Particle Sizer Spectrometers (SMPS).

The likelihood of exposure has been classified in low, possible and high considering the increase in the concentration of ENMs compared to the background measurement. An alternative method can be based on the comparison with recommended exposure levels (REL) proposed by international organisations such as BSI (British Standards Institution, UK), IFA (Institut für Arbeitsschutz, DE), NIOSH (The National Institute for Occupational Safety and Health, USA), SWA (Safe Work Australia, Australia) or AIST (National Institute of Advanced Industrial Science and Technology, Japan).

It can be seen how the most possible scenarios of having exposure are the ones where the substance is manipulated in powder form, independently of the material chemical composition, although is not determinant, since there are examples of high energetic processes with powdered forms in which the possibility of exposure is low, probably due to a good system of risk management measures. Therefore, each case must be carefully investigated to extract the assessment of the exposure.

The categories of potentially exposed workers include production operators, R&D scientists, technicians, quality testing staff, general maintenance personnel, waste handling workers, packaging personnel, or recycling plant workers among others.



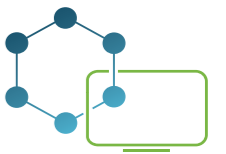
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Table 6. Examples of levels of exposure to NMs in workplaces for different life cycle stages

LIFECYCLE STAGE	WORKPLACE ACTIVITIES	ENMS TYPE			BACK-GROUND	ACTIVITY	OBSERVATIONS		SCALE OF RISK OF EXPOSURE	
		ENMS	PHYSICAL STATE	PRIMARY PARTICLE SIZE (nm)			#/CM ³	INSTRUMENT		DURATION (MIN)
Synthesis	Weighing, mixing, transferring	SWCNT	powder and liquid suspension	80-100 µm	3187	4379			Low probability	
	Synthesis	Carbon fibre	Film, fibre	50-200 nm	1500000	250000	FMPS	60	Low probability	
	Machining (sawing, grinding)	SiO ₂			13228	77476	CPC	6	Possible	
	Pyrolysis	TiO ₂	Powder	> 40 nm	34537	38021	FMPS	120	Low probability	
	Production (Physical and chemical synthesis)	TiO ₂	Solid	20-80 nm	11974	11699	SMPS		Low probability	
	Production (Physical and chemical synthesis)	ZnO	Paste	> 40 nm	5541	5911	FMPS		Low probability	
	Production (Physical and chemical synthesis)	MWCNT	Powder	Length < 5 µm	2550		Nano Tracer		Low probability	
	Production (Physical and chemical synthesis)	MWCNT	Powder	Length < 5 µm	7400		Nano Tracer		Low probability	
	Formulation and incorporation	Spraying	Ag			18642	25936	CPC	7	Possible
		Spraying	Ag			18000	32477	CPC		Possible
Spraying		AlO ₂	Liquid dispersion containing the nanoparticles	20-50 nm	84708	65468	CPC	30	Low probability	
Spraying		CeO ₂	Powder	11-40 nm	4600	210000	SMPS	90	Possible	
Spraying		SiO ₂	Powder	20-30 nm	4600	210000	CPC	16	Possible	
Spraying		TiO ₂		21 nm	1298	942	DISCmini	13	Low probability	
Spraying		ZrO ₂	Powder	3 nm	3000	3788	CPC		Low probability	
Weighing, mixing, transferring		TiO ₂	Powder	80 ± 50 nm		504.1	Cascade impactor	458	Low probability	
Weighing, mixing, transferring		TiO ₂	Powder	11-40 nm	16918	17687	FMPS	86	Low probability	
Weighing, mixing, transferring		Carbon black	Powder	11-40 nm	8304	9598	CPC	30	Low probability	
Machining (sawing, grinding)		Nanoclays	Powder		300	1100	SMPS		Possible	
Extrusion		CNT	Powder	Length: 1.5 µm; inner d.: 2-6 nm	44839	23045	FMPS	137	Low probability	
Extrusion		CNT	Pellet	Length: 1.5 µm; inner d.: 2-6 nm	44839	30116	FMPS	137	Low probability	
Extrusion		CNT	Solid Object	Length: 0.5 µm; inner d.: 19 nm	11086	24666	CPC	30	Possible	
Cleaning		Carbon black			1717	5898	CPC	10	Possible	

LIFECYCLE STAGE	WORKPLACE ACTIVITIES	ENMS TYPE			BACK-GROUND	ACTIVITY	OBSERVATIONS		SCALE OF RISK OF EXPOSURE
		ENMS	PHYSICAL STATE	PRIMARY PARTICLE SIZE (nm)			#/CM ³	INSTRUMENT	
Manufacture of end product	Machining (sawing, grinding)	Ag			10141	10441	CPC	16	Low probability
	Coating	Ag	Solid tile or brick	3-8 nm	13210	10885	CPC	16	Low probability
	Coating	Ag	Liquid		44891	127296	CPC	18	Possible
	Spraying	Ag	Liquid	45 ± 8 nm	1530	1594	CPC	16	Low probability
	Spraying	TiO ₂	Liquid	20-30 nm	35006	60809	CPC	23	Possible
	Spraying	TiO ₂	Liquid	20-30 nm	61439	25167	Nanotracer	23	Low probability
	Spraying	TiO ₂	Liquid	44-57 nm	13500	15087	CPC	3	Low probability
	Spraying	TiO ₂	Liquid	44-57 nm	15087	18670	CPC	8	Low probability
	Spraying	ZnO	Liquid	25 nm	13388	55906	CPC	15	Possible
	Coating	TiO ₂	Liquid	20 nm	168453	140193	CPC		Low probability
	Weighing & Mixing	ZnO	Powder	> 40 nm	16918	17687	FMPS	29	Low probability
	Weighing, mixing, transferring	TiO ₂	Powder		6242	6272	SMPS		Low probability
	Weighing, mixing, transferring	TiO ₂	Powder		16509	16285	CPC		Low probability
	Weighing, mixing, transferring	ZnO	Powder		6242	6272	SMPS		Low probability
	Weighing, mixing, transferring	Graphene		50 nm	600	1800	Nanotracer		Possible
End of Life	Machining (sawing, grinding)	SiO ₂	Paste	20 nm	6296	5449	CPC	16	Low probability
	Machining (sawing, grinding)	Ag	Solid Object	70 nm	1876	5030	AeroTrak	16	Possible
	Machining (sawing, grinding)	Cu	Solid Object		5199	5030	CPC	16	Low probability
	Machining & abrasion	ZrO ₂	Paste	11-40 nm	6296	5449	CPC	16	Low probability

Scale of Risk of Exposure: Low probability Possible High probability



3. ANALYSIS OF CURRENT KNOWLEDGE ON THE CONCENTRATION LEVELS OF ENMS IN INDOOR WORKPLACES AND THE ENVIRONMENT

3.3 Levels of exposure in urban areas

The International Organization for Standardization (ISO) defines PM10 as particles which pass through a size-selective inlet with a 50 % efficiency cut-off at 10 µm aerodynamic diameter, while PM2.5 are particles which pass through a size-selective inlet with a 50 % efficiency cut-off at 2,5 µm aerodynamic diameter (ISO 23210:2009).

Potential danger to human health from exposure to PM10 and PM2.5 particulate matter has been studied for years. It is considered in the Directive 2008/50/EC of 21 May 2008 of the European Parliament on Ambient air quality and a cleaner atmosphere, which defines their maximum permissible concentrations and the measures to be taken if they are exceeded.

But PM10 and PM2.5 are not the only particulate fractions present in the atmosphere. In a similar way, PM1 or PM0.1 can be defined. Aerosols included in PM0.1 and below are considered nanoparticles. Smaller particles have a higher potential risk for human health since their small size allows them to penetrate deeply into the respiratory tract, reaching the pulmonary alveoli level.

Since nano-risk is a relatively new topic, still a few studies are conclusive regarding the relationship between health problems and nanoparticle concentration. As a consequence, nowadays there is a lack of legislation for PM1 or PM0.1.

However, it is reasonable to think that, since there is a regulation applicable to PM10 and PM2.5 for outdoor environments, in the near future, air quality regulations will be developed in a similar way for fractions of particulate material below 1 micron.

All outdoor studies on PM in the atmosphere agree that only a fraction of the total amount of particulate matter present in the (outdoor) atmosphere has an anthropogenic origin; and therefore, a significant fraction should be considered as a "natural" background (EEA Technical report/N° 10/2012). In addition, this natural contribution to the total suspended particles in the atmosphere is more significant in arid and semi-arid regions, in coastal areas, and also in the regions downwind big desert areas (as is the case of the Mediterranean regions, north of the Saharan desert). Wind blowing over arid zones creates mineral dust particles (Grini et al., 2002), while sea spray aerosols are generated in the oceans by a combination of wind speed and the sea water movement (Ryu et al., 2007; Pósfai and Molnár, 2000). However, generally speaking, natural aerosols affect a relatively small percentage of world population.

Other natural phenomena, such as volcanic eruptions, have a contribution and affect a local or a wider area, depending on the violence of the eruption (Vernier et al., 2011). Furthermore, lightning is an important source of NO_x (NO and NO₂) in the atmosphere and as a consequence another source of particles, specifically, secondary natural nitrate particles (Schumann and Huntrieser, 2007).

Even with all the above, the main contribution of particulate matter in the lower atmosphere (troposphere) comes from human activity (anthropogenic sources). Industrial processes and road traffic are the main sources, but coal burning in coal power plants (Tsitouridou and Anatolaki, 2007) or in residences (e.g. Chen et al., 2009; Shen et al., 2010), biomass burnings (from wildfires with emissions characterised by aircraft, satellite and ground-based measurements (Cook et al., 2007; Janhäll et al., 2010; Knobelspiesse et al., 2011; Urbanski et al., 2011), domestic uses and agriculture activities (Ortiz de Zárate et al., 2005)) or even food cooking (Buonanno et al., 2009), play an important role in the total amount of aerosols released.

Emissions from road traffic come mainly from the engine exhausts but also from tyres (Dahl et al., 2006), brakes (Sanders et al., 2003) and waste oils. The concentration of particles released by traffic and their composition has been the object of study for many authors (e.g. Fang et al., 2006; Martuzevicius et al., 2008)

In a lower scale, railway (Lorenzo et al., 2006), air (Miracolo et al., 2011) and maritime (Kim et al., 2009) traffic have also a contribution to the emissions of particulate matter. In specific, for many industrial processes, the use of ENMs is growing exponentially, due to the research in new applications where they play a fundamental role. Its use is spreading, and as a consequence, the exposure risk for population is increasing. Potentially, these industries could release nanomaterials to the atmosphere, becoming new sources of particulate matter.

In addition to these primary aerosols (emitted directly from a source), human activity is also responsible for emission of precursors, mainly nitrates (e.g. Pinder et al., 2012) and sulphates (e.g. Penner, 2001), which through atmospheric reactions with other chemical compounds in the presence of sunlight, become aerosols too. These are the secondary aerosols.

The aforementioned processes not only contribute in a great way to the particle number concentration in the atmosphere, but in addition, they usually take place in densely populated areas. So, they could have a direct negative effect on the inhabitants' health in these areas.

Simultaneously with the increase of devices and processes based on the use of nanomaterials, new instruments capable of measuring the airborne particle number concentration and/or the mass concentration in the range of nanometers have been developed. These instruments could be used to measure concentration, distribution or composition of nanoparticles in air samples, and therefore, to assess the associated risk in an environment. Table 7 shows some typical inorganic markers associated to a source or process.

Table 7. Inorganic marker elements associated with various emission sources or processes (Calvo et al., 2013).

Secondary aerosols	SO ₄ ²⁻ , NO ₃ ⁻ , NH ₄ ⁺	
Sea Salt	Cl, Na, Na ⁺ , Cl ⁻ , Br, I, Mg and Mg ²⁺	
Crustal or geological tracers	Elements associated with feldspars, quartz, micas and their weathering products (mostly clay minerals), i.e. Si, Al, K, Na, Ca, Fe and associated trace elements such as Ba, Sr, Rb and Li. In addition, there will be accessory silicates (notably zircon, titanite and epidote), and representatives from the minority non-silicate mineral groups, namely carbonates, sulphates, oxides, hydroxides and phosphates.	
Technogenic tracers	Steel industry	Cr, Ni and Mo
	Copper metallurgy	Cu and As
	Ceramic industries	Ce, Zr and Pb
	Heavy industry (refinery, coal mine, power stations)	Ti, V, Cr, Co, Ni, Zn, As and Sb
	Petrochemical industry	Ni and V
	Oil burning	V, Ni, Mn, Fe, Cr, As, S and SO ₄ ²⁻
	Coal burning	Al, Sc, Se, Co, As, Ti, Th, S, Pb and Sb
	Iron and steel industries	Mn, Cr, Fe, Zn, W and Rb
	Non-ferrous metal industries	Zn, Cu, As, Sb, Pb and Al
	Cement industry	Ca
	Refuse incineration	K, Zn, Pb and Sb
	Biomass burning	K and Br
	Firework combustion	K, Pb, Ba, Sb and Sr
	Vehicle tailpipe	Platinum group elements, Ce, Mo and Zn
	Automobile gasoline	Ce, La, Pt, SO ₄ ²⁻ and NO ₃ ⁻
Automobile diesel	S, SO ₄ ²⁻ and NO ₃ ⁻	
Mechanical abrasion of tyres	Zn	
Mechanical abrasion of brakes	Ba, Cu and Sb	

The specialised bibliography describes different technologies and methodologies to measure particulate matter (including nanoparticles) depending mainly on the objectives of each specific study and/or environmental assessment, as well as the available instrumentation.

Some of them, studying environmental scenarios where the most part of the population is exposed to emissions from road traffic (specifically to particles emitted from engines, exhausts or brakes) start characterising such emissions depending on the type of vehicle (car, truck, bus, etc.), type of fuel used (diesel or gasoline) and type of brakes.

Other studies analyse emissions from road traffic in one (or more) specific way, motorway, traffic tunnel, street or route(s). Within this second category of studies, a wide range of possibilities for carrying out such measurements is documented.

Instruments are placed in a fixed location during a period of time to monitor the particulate matter concentrations when that specific location is downwind/upwind from the emission sources. This strategy also makes it possible to record the diurnal/nocturnal oscillation, the weekly variability (weekdays versus weekend or/and even seasonality (summer versus winter conditions)). Generally, studies following this methodology are complemented with measures of concentration of other relevant atmospheric pollutants and meteorological variables (wind speed and direction, temperature, etc.).

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Instruments are installed in a vehicle, measuring while the automobile is traveling along a predefined route. This methodology makes it possible to assess the atmospheric concentration in different areas during the day, identifying hot spots and/or monitoring specific emission and dispersive scenarios: tunnels, traffic jams, industrial parks, etc.

Since industrial areas are another important source of particulate matter, it is of special interest (more often if these industrial areas are close to urban areas) to identify the chemical composition of the particles in addition to the measure of the concentrations. Again, access to meteorological information becomes critical in order to identify where the measured particles come from or/and to estimate the fate of the emissions.

For epidemiological studies, in which the aim is to quantify the human being's exposure to the concentration levels in a given environment (urban, industrial, domestic, etc.), portable monitors are carried by volunteers following a certain routine (or habit) such as, for example, riding a bicycle through the city, walking, working indoors/outdoors, working in schools, being in hospitals, etc. The aim of this methodology is to measure concentrations representative of the levels of exposure of a specific population sector.

Some examples of the different methodologies and scenarios described above, as well as their associated concentration levels, can be found in Table 8. It summarises the measured concentrations of particulate matter obtained in different cities around the world.

Although, in most cases listed in Table 8, the main sources are vehicle exhaust emissions it is important to note that it is not a trivial exercise to carry out a direct comparison among them and that the conclusions reached could be meaningless. This is mainly due to the fact that the measurements published in the specialised bibliography are very heterogeneous in terms of the instrumentation used, the variables measured, the size range covered, the location of the instruments and the measurement periods.

Table 8. Measured levels of nanoparticles in urban areas

URBAN COMPARTMENT	LOCATION	MAIN PARTICLE SOURCE	MEASURED CONCENTRATION	OBSERVATIONS		SOURCE
				INSTRUMENT	OTHERS	
Outdoor	Somerville (USA)	Traffic road emissions	Median PNC $3.7 \times 10^4 \text{ cm}^{-3}$ Median BC $1000 \mu\text{g}/\text{m}^3$ Median PM _{2.5} $16 \mu\text{g}/\text{m}^3$	CPC Aethalometer LP	Mobile monitoring platform	Padró-Martínez et al., 2012
Outdoor	Birmingham (UK)	Traffic road emissions	Max PNC Average $(9.5 \pm 3.5) \times 10^4 \text{ cm}^{-3}$ Max PNC Average $(1.7 \pm 0.5) \times 10^5 \text{ cm}^{-3}$	CPC UCPC	Three different sampling sites	Shi et al., 2001
Outdoor	Barcelona (Spain)	Traffic road emissions	PNC [3204 – 11946] cm^{-3} BC [1529 – 9214] ng/m^3 PM ₁ [5.2 – 23.9] $\mu\text{g}/\text{m}^3$	DisCMini Aethalometer Dusttrack	Comparison at a fixed place	Viana et al., 2015
Outdoor	Brisbane (Australia)	Traffic road emissions Industrial / Maritime	Max PNC Average $45.6 \times 10^3 \text{ cm}^{-3}$ Max PNC Average $13.2 \times 10^3 \text{ cm}^{-3}$	CPC	Nine locations around Brisbane	Mejía et al., 2008
Outdoor	Cassino (Italy)	Traffic road emissions	Max PNC Average $5.0 \times 10^4 \text{ cm}^{-3}$	CPC FMPS APS	Measurements were taken by simulating four pedestrian routes	Buonanno et al., 2011
Outdoor	Montelibretti (Italy)	Traffic road emissions	Daily Average PNC 19000 cm^{-3}	CPC	Characterisation of a semi-rural area	Wang et al., 2010
Outdoor	Helsinki (Finland)	Traffic road emissions	Max Average LDSA $94 \mu\text{g}/\text{cm}^3$ Min Average LDSA $12 \mu\text{g}/\text{cm}^3$	NSAM	Both, stationary and mobile lab measurements	Kuuluvainen et al., 2016

URBAN COMPARTMENT	LOCATION	MAIN PARTICLE SOURCE	MEASURED CONCENTRATION	OBSERVATIONS		SOURCE
				INSTRUMENT	OTHERS	
Outdoor	New York (USA) City and State	Traffic road emissions	PNC [280 – 160] $\times 10^3 \text{ cm}^{-3}$ PNC [5.6 – 3.5] $\times 10^3 \text{ cm}^{-3}$	CPC	Urban environment Rural environment	Bae et al., 2010
Outdoor	Helsinki (Finland)	Traffic road emissions	PNC [43000 – 12000] cm^{-3} PNC [6000 – 4000] cm^{-3}	CPC	Urban environment Rural environment	Hämeri et al., 2004
Outdoor	Helsinki	Traffic road emissions	Total PNC 16660 cm^{-3}		Urban environment	Laakso et al., 2003
Outdoor	Värrio		Total PNC 2110 cm^{-3}		Rural environment	
Outdoor	Pallas		Total PNC 920 cm^{-3}		Arctic environment	
Indoor	Los Ángeles (USA)	Traffic road emissions	PNC [12000 – 9000] cm^{-3}	P-Track UPC	Measurements were taken in four apartments (indoor/outdoor), as well as day and night time	Zhu et al., 2005
Outdoor			PNC [20000 – 14000] cm^{-3}			
Outdoor	Seoul (South Korea)	Traffic road emissions	Mean PNC 93000 cm^{-3}	FMPS	On-road measurements using a mobile lab	Kim et al., 2015
Outdoor	Ontario (Canada)	Traffic road emissions	Average PNC [36800 – 11400] cm^{-3}	FMPS	Urban environment	Sabaliauskas et al., 2012
Outdoor	Barcelona (Spain)	Mainly traffic road emissions, but contributions of industry and natural sources (dust) in some locations	PNC [29449 – 6140] cm^{-3}	CPC	Urban, urban background and industrial environments covered	Reche et al., 2011
	Lugano (Switzerland)		PNC [47562 – 2751] cm^{-3}			
	Bern (Switzerland)		PNC [93078 – 8888] cm^{-3}			
	London (UK)		PNC [58017 – 4753] cm^{-3}			
	Huelva (Spain)		PNC [67949 – 1091] cm^{-3}			
Outdoor	Sta Cruz de Tenerife (Spain)	PNC [26294 – 1076] cm^{-3}				
Outdoor and Indoor	Milan (Italy)	Traffic road emissions	Max PNC 100200 cm^{-3} (Walking time) Max PNC 117600 cm^{-3} (Bus) Max PNC 107000 cm^{-3} (Car) Max PNC 23400 cm^{-3} (Green areas) Max PNC 13500 cm^{-3} (Office, Indoor)	CPC	Date were collected following paths afoot or by public or private means of transport, as well as in the office (indoor)	Cattaneo, 2009
Outdoor	Mol (Belgium)	Traffic road emissions	PNC [122000 – 5429] cm^{-3} PM ₁ [105 – 6,07] $\mu\text{g}/\text{m}^3$	Spectrometer P-Track UPC	Measurements of the exposure of a cyclist	Berghmans et al., 2009
Outdoor and Indoor	Brisbane (Australia)	Traffic road emissions	PNC [10500 – 1000] cm^{-3}	Nanotracer	A group of children carried personal monitors 24h while do their activities	Clifford et al., 2014
Outdoor and Indoor	Athens (Greece)	Traffic road emissions	Mean PNC Residence 13000 cm^{-3} Mean PNC School 13200 cm^{-3} Mean PNC School 13200 cm^{-3} Mean PNC in- vehicle morning/afternoon rush $79600/52700 \text{ cm}^{-3}$	CPC	Comparison of exposure to NP indoors (schools and residences) and outdoors (while driving)	Diapouli et al., 2007

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3.4 Environmental levels of ENMs in the environment

3.4.1. Water compartment

Current data on the concentration of ENMs is still scarce due to current limitations to detect and measure ENMs in natural environments. Detection of ENMs in natural water systems is very challenging and suitable analytical methods are still under development (Klaine et al., 2012; von der Kammer et al., 2012)

The vast majority of the data can be retrieved from modelling studies, with values ranging from 0.0058 to 150 ng /L. Figure 4 shows the arithmetic mean and the range of predicted environmental concentration (PEC) values retrieved from modelling and analytical studies. As can be derived from the figure, a higher concentration of nano-ZnO can be expected according with current studies, ranging from 3 µg/L to 76 µg/L.

Table 9 shows a non-exhaustive list of data published in recent years.

In the case of water compartments, it can be observed that there are nanoparticles that concentrate most of the attention according to the analysed bibliography: TiO₂, ZnO, Ag Nps and CNT. Other nanoparticles, like CeO₂, gold nanoparticles, CuCO₃ or SiO₂ seems that have not been studied too much yet.

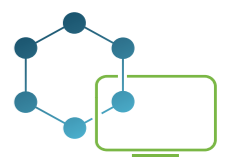
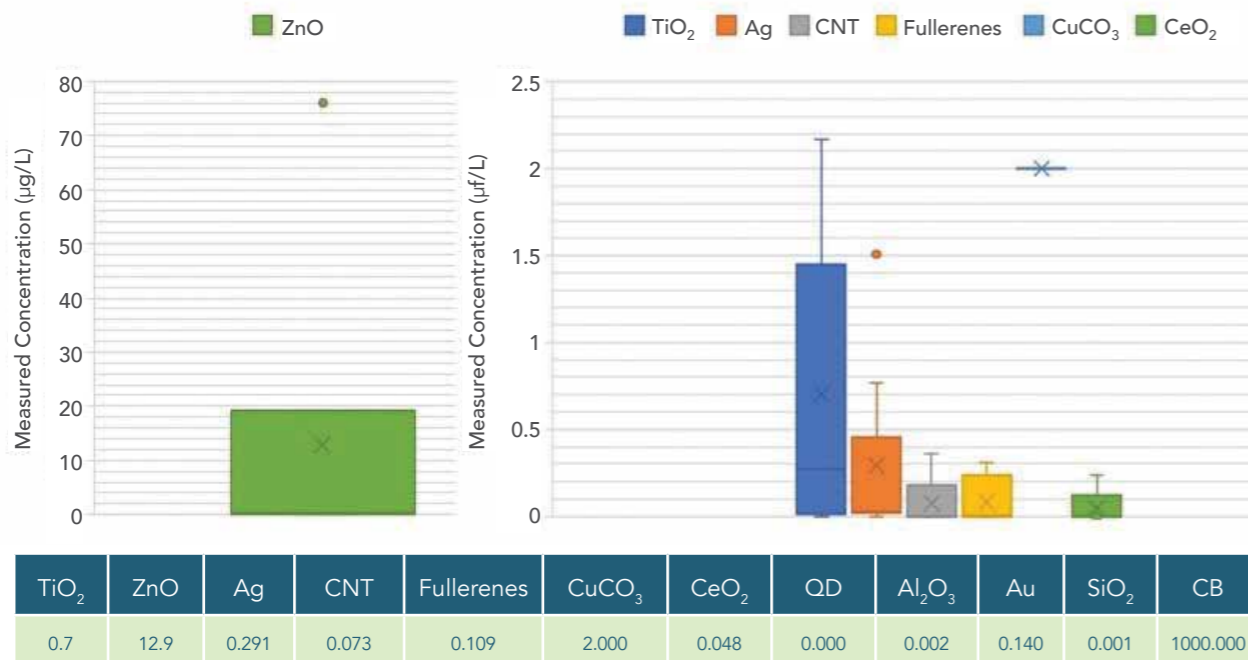
However, there are large differences regarding the concentration depending on the performed study. This may be due of the transformations of nanomaterials, such as dissolution, agglomeration, sedimentation, or change of surface moieties, which could greatly affect the pathway and extent of environmental release.

Table 9. Estimated concentrations of ENMs in water

ENMs	WATER Estimated									
	Gottschalk, 2009	T.Y. Sun, 2016	Gottschalk, 2015	Gottschalk, 2013	Gottschalk, 2011	Muller and Nowack, 2008	Jones et al., 2007	Blaser et al., 2008	Batley and McLaughlin, 2010	O'Brien and Cummins, 2014
TiO ₂	0.015 µg/L	2.17 µg/L	0.27* µg/L	< 1 µg/L	< 0.01 µg/L	0.7 *10 ⁻³ µg m ⁻³			24.5 µg /L	1.45 µg /L
ZnO	0.010 µg/L	0.38 µg/L	0.45 µg/L	< 0.1 µg/L	< 0.5 µg/L				76 µg /L	
Ag	0.764 µg/L	1.51 µg/L	< 0.001 µg/L	< 0.1 µg/L	< 0.03 µg/L	0.03 µg L ⁻¹		140 ng/L	0.01 µg /L	0.03 µg /L
CNT	0.004 µg/L	0.36 µg/L	< 0.001 µg/L	< 0.001 µg/L		0.0005 µg L ⁻¹				
Fullerenes	0.017 µg/L			< 0.0001 µg/L					0.31 µg /L	
CuCO ₃			2 µg/L							
CeO ₂			< 0.001 µg/L	< 0.001µg/L			<1 ng/L		<0.0001 µg /L	0.24 µg /L
QD			< fg							
Al ₂ O ₃									0.002 µg /L	
Au									0.14 µg /L	
SiO ₂									0.0007 µg /L	
CB			>1000 µg/L							
Source	Gottschalk, 2009	T.Y. Sun, 2016	Gottschalk, 2015	Gottschalk, 2013	Gottschalk, 2011	Muller and Nowack, 2008	Jones et al., 2007	Blaser et al., 2008	Batley and McLaughlin, 2010	O'Brien and Cummins, 2014

* Photocatalytic TiO₂

Figure 4. Modelled and analytical concentrations of ENMs in surface waters.



3. ANALYSIS OF CURRENT KNOWLEDGE ON THE CONCENTRATION LEVELS OF ENMS IN INDOOR WORKPLACES AND THE ENVIRONMENT

3.4.2. Soil compartment

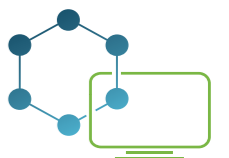
ENMs can enter soils through various sources and pathways such as the application of fertilisers and plant protection products (Batley et al., 2013), biosolids (Benn and Westerhoff, 2008), the irrigation of sewage water (Gottschalk et al., 2009) or the flooding of floodplains (Lecoanet et al., 2004).

As in the case of surface water, a limited number of studies provide information on the concentration of ENMs in soils. It shall be noted that ENMs can be found associated with their inorganic counterparts or form coatings over mineral surfaces. For this reason, individual ENMs are difficult to separate and collect from the bulk soil.

Apparently, only a small proportion of nanoparticles in soil occur as discrete entities. Organic colloids in soil, for example, are largely associated with their inorganic counterparts or form coatings over mineral surfaces. For this reason, individual nanoparticles are difficult to separate and collect from the bulk soil, and extraction yields are generally low. By the same token, the characterisation of soil nanoparticles often requires advanced analytical and spectroscopic techniques. Because of their large surface area and the presence of surface defects and dislocations, nanoparticles in soil are very reactive towards external solute molecule. Table 10 shows measured modelled concentrations of ENMs in soils.

Table 10. Estimated concentrations of ENMs in soil ENMs SOIL Estimated

ENMs	SOIL Estimated				
TiO ₂	1.5 µg/L	>100 µg/L	0.4 µg kg ⁻¹		1030 µg /kg
ZnO	0.12 µg/L	>100 µg/L			3190 µg /kg
Ag	0.024 µg/L	>1 µg/L	0.02 µg kg ⁻¹		1.45 µg /kg
CNT	0.083 µg/L	>100 µg/L	0.01 µg kg ⁻¹		
Fullerenes		< 0.1 µg/L			44.7 µg /kg
CuCO ₃	60 µg/L				
CeO ₂	0.170 µg/L			<0.01 mg/kg	0.01 µg /kg
QD	nq				
Al ₂ O ₃					0.01 µg /kg
Au					20.4 µg /kg
Source	Gottschalk, 2015	Gottschalk, 2013	Muller and Nowack, 2008	Jones et al., 2007	Batley and McLaughlin, 2010



4. RECOMMENDATIONS FOR EXPOSURE ASSESSMENT OF ENGINEERED NANOMATERIALS IN THE WORKPLACE

4.1 Introduction

Current strategies to conduct an exposure assessment in the workplace are based on a tiered approach, ranging from a qualitative analysis to the combination of an array of field portable, direct reading instruments in combination with filter-based air sampling and subsequent laboratory analysis.

A harmonised tiered approach to measure and assess the potential exposure to ENMs and their agglomerates and aggregates at workplaces is given in (OECD, 2015). This approach comprises three subsequent steps ("tiers"), which mainly aim to deal with the problem that many of the instruments used to detect and measure engineered nanomaterials (ENMs) are non-specific, i.e. they cannot distinguish the ENMs from ambient nano-size particles "background". The National Institute for Occupational Safety and Health (NIOSH) from USA has also been researching this issue for over a decade. In 2016, this entity published a refined version of the earlier published Nanoparticle Emission Assessment Technique (NEAT 1.0).

In October 2017, a new report on strategies, techniques and sampling protocols for determining the concentration of ENMs in air at the workplace was published (ENV/JM/MONO(2017)30), describing three-tiered assessment process to conduct the evaluation of the exposure by inhalation. Other exposure routes such as dermal may also be important and should be evaluated where possible.

This chapter outlines a recommended strategy to support the assessment of the potential exposure to ENMs in industrial facilities. This strategy is based on the three-tiered Approach for Nanomaterials Emissions and Exposure Measurement published by the OECD in 2017, involving:

- Tier 1. Information gathering to determine potential sources of release of ENMs. Involves a standard industrial hygiene survey of the process area and is predominantly focussed on gathering qualitative information, with some quantitative measurement, to identify likely points of particle emission.
- Tier 2. Assessment of the release of ENMs into the workplace air form identifies sources using handheld particle counters such as CPCs, which enable the assessment of particle number concentration in the emission sources, breathing zone exposure of process operators, incidental and background particles.
- Tier 3. When a release of ENMs has been observed, additional information may need to be determined on whether or not exposure to ENMs can be excluded. In this step, appropriate equipment beyond easy-to-use particle counters must be employed. This step generally involves the use of a SMPS to access the particle size distribution, as well as filter-based sampling (i.e., elemental mass analysis and particle morphology) in the worker's breathing zone.

Results from either Tier 2 or Tier 3, or both, can be compared with particle control values for decision-making about controls. The measurement of background particle number concentration is of prime importance at industrial situations in order to support the definition of a benchmark value for deciding when control of human exposure is required. This is not an occupational exposure limit (OEL) or Workplace Exposure Standard (WES), but is intended as a pragmatic guidance level. Figure 5 depicts the recommended three-Tiered approach for the ENMs exposure assessment in the workplace.

The monitoring station developed under NanoMONITOR can be used in Tier 2 and Tier 3 assessments as the station provides particle number concentrations and allows filter-based sampling for electron microscopy characterisation (e.g. shape, size, identification).

Figure 6 show CAD drawing of the NanoMONITOR monitoring station. The device includes three sampling channels controlled by electro valves to achieve a constant flow rate ranging from 5 to 30 LPM. This design allows the use of open-face filter cassettes, cascade impactor, and cyclones, in order to provide chemical composition information which cannot be obtained from online instrumentation.

Figure 5. Tiered approach for the ENMs exposure assessment in the workplace

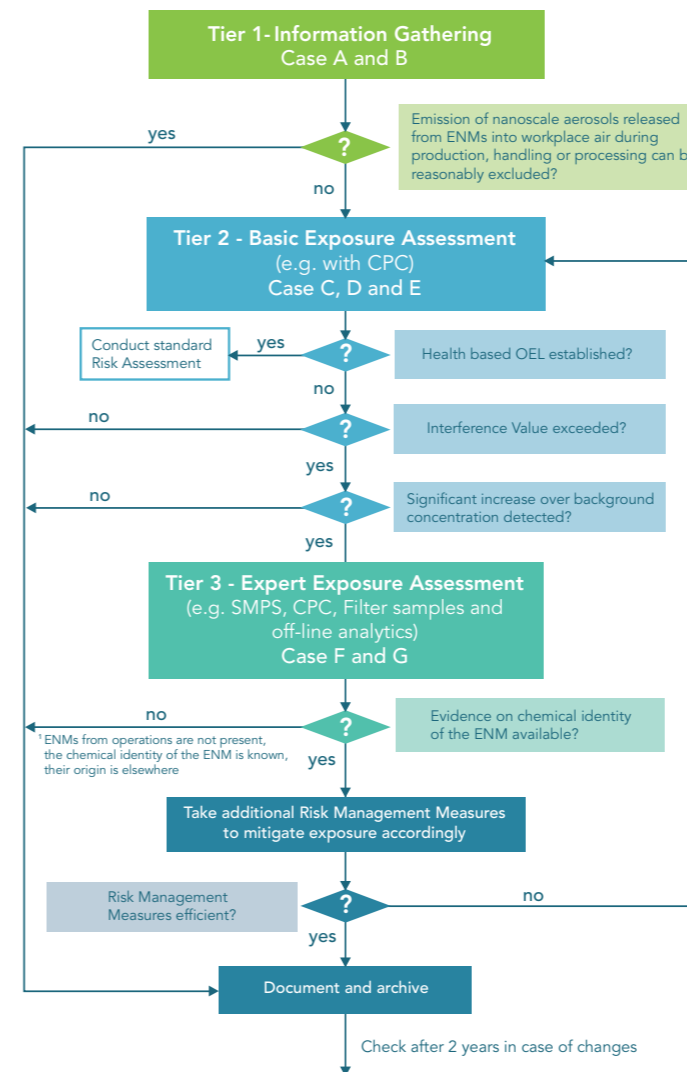
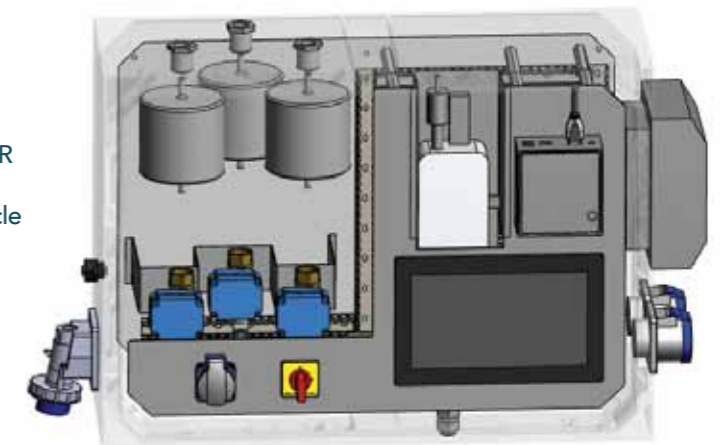


Figure 6. View inside the different parts of the NanoMONITOR station. Left: sampling system with space for up to three independent setups. Right: sensor system with the nanoparticle monitoring device and the software and interface to connect the station.



4. RECOMMENDATIONS FOR EXPOSURE ASSESSMENT OF ENGINEERED NANOMATERIALS IN THE WORKPLACE

4.2 Step by step guidance

Step 1. Information gathering

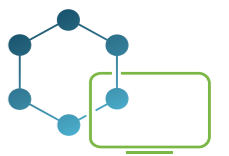
The overall purpose of this step is to develop a list of target areas, processes, or tasks that will be evaluated with the direct reading instrumentation. The initial assessment involves identifying the potential source(s) of ENMs emissions by reviewing the type of process, process flow, material inputs and discharges, and work practices.

This step can be conducted using specific questionnaires to collect relevant data on the determinants of exposure. These questionnaires have to include data on the characteristics of the ENPs, as well as contextual information on the operative conditions and risk controls applied.

An example a questionnaire designed by ITENE is included below:

ADMINISTRATIVE / COMPANY INFORMATION	
Company name	
Contact name	
Telephone number (country and regional codes)	
Loss of containment	
E-mail	
Industrial Sector	
ACTIVITY INFORMATION	
Type of nanomaterials your company handle or produce	- Form (dispersion, powder, etc.) - Size and shape - Type (platelets, fibres, spheres, etc.): - Characteristics: metal, metal oxide, carbonaceous, ...
List the different types of ENMs or products containing ENMs that are handled at your company	- ZnO - CaCO ₃ - Ag
Type of processes in your company in which ENMs or products containing ENMs are used or present	1. Production of nanomaterials by Sol-gel 2. Cleaning operations
PROCESS INFORMATION	
PROCESS 1:	ENMS COMPOUNDING
Process Description (indicating the steps where the ENPs or products containing ENMs are handled)	ENPs compounding by twin-screw extrusion
In what physical form are the ENMs or products containing ENPs handled (powders, pellets, solution)	Powder
In what type of packing is the ENM received or packed after synthesis	Plastic bag
How are the ENPs transferred to the production line (e.g. automatic feeder, manual)?	Manual feeding
Total amount of ENPs used/produced per shift	300 mg
What is the end-product for this process?	Nanocomposites

PROCESS INFORMATION	
TASKS WITHIN PROCESS 1 (CONTRIBUTION SCENARIO N° 1)	HOOPER FEEDING
Physical form of the ENM	Powder
Amount used	150 mg
Ventilation system	Local exhaust ventilation
Volume of the room	20 m ³
Level of automation	Manual
Level of containment	Open when feeding and close when operating
Exposure duration	10 min/h of work
Effectiveness and types of PPE used	95 %
TASKS WITHIN PROCESS 1 (CONTRIBUTION SCENARIO N° 2)	CLEANING OPERATIONS
Physical form of the ENM	Powder
Amount used	N.A
Ventilation system	Local exhaust ventilation
Volume of the room	20 m ³
Level of automation	Manual
Level of containment	Open
Exposure duration	5 min/h of work
Effectiveness and types of PPE used	95 %



4. RECOMMENDATIONS FOR EXPOSURE ASSESSMENT OF ENGINEERED NANOMATERIALS IN THE WORKPLACE

Step 2. Definition of the measurement strategy

The second step will focus on the definition a clear measurement strategy based on the information retrieved from the questionnaires. A measurement strategy can be described as a framework for the selection of relevant considerations associated with a measurement campaign (e.g. what ENM will be measured, at which location, when, for how long, how many individuals to sample, how many samples per individual to collect, and by what methods, in particular, what exposure metrics will be measured).

The first stage when organising a measurement campaign is to plan the activities to be conducted on site and select the instrumentation and materials needed to evaluate the exposure. The data and samples collected on site will be analysed off-site by means of different techniques and data management software. The recommend steps to follow are described below:

1. Planning: the planning stage involves determining the measurement strategy as well as identifying the nature and the timing of the activities to be performed. This is done to optimise efficiency and effectiveness when conducting the measurements

2. Selection of instrumentation and materials: there are a wide range of measurement and sampling devices for airborne ENPs used in workplace studies. The following table summarises common devices used for risk assessment purposes.

Researchers in aerosol technology commonly use the instruments included in table x. However, few of the abovementioned instruments are used to evaluate the exposure at industrial facilities due to the lack of filed portability, complexity of use, and high cost.

Up to date, following recommended methodologies from key researches, the instruments that can provide valuable information are:

- Handheld Condensation Particle Counter in the size range of 10 to 1000 nm
- Handheld Optical Particle Sizer in the size range of 0.3 to 10 μm
- Transportable Particle Sizer. Depending on the time resolution needed, SMPS-Scanning mobility particle sizer (<30 s) or the FMPS-Fast mobility particle sizer (1 s)
- Transportable surface area monitor in the size range of 10 nm to 1000 nm

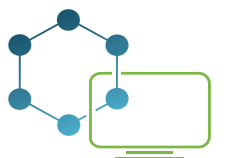
The combined use of these instruments will provide valuable information on the levels of exposure to airborne ENMs, including particle number concentration, size distribution and surface area, all relevant metrics for risk assessment.

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 ENP and desired analytical information. In this sense, traditional open-faced cassettes (37 mm) are used.

The monitoring station developed under NanoMONITOR is equipped with a OM version of a DISCmini, a handheld sensor for the measurement of nanoparticle number, average diameter and lung-deposited surface area LDSA with a time resolution of up to 1 second (1 Hz). The concentration range is from about 1'000 to over 1'000'000 particles per cubic centimeter. The accuracy of the measurement depends on the shape of the particle size distribution and number concentration, and is usually around 15-20% compared to a reference CPC.

Table 11. Measurement and sampling devices for airborne nanomaterials

INSTRUMENT	METHOD	TYPE	REMARKS
Particle Counters (PC)	Heated saturator	Size integrated CPC	Particle counter intended for measuring ultrafine particles (10 – 100 nm) Concentration range of 0 to 100,000 particles/cm ³ Metrics: particle number concentration (PNC)
	Diffusion charging	Size resolved Nanotracers	Detects ultra-fine airborne particles (10 to 300 nm) Concentration range of 0 to 1.106 particles/cm ³ Measures both particle concentration (PC) and average particle diameter (APD)
Optical Particle Sizer / Laser aerosol spectrometer	Laser light scattering	Size resolved OPS LAS	Provides fast and accurate measurement of particle concentration and particle size distribution (300 nm – 10 μm) Metrics: number size distribution
Surface Area monitor	Diffusion charging	Size integrated NSAM	Provides fast and accurate measurement of active particle surface area / Size range: 10 nm – 1 μm) Concentration range: 0 to 10,000 $\mu\text{m}^2/\text{cm}^3$ Metrics: surface area reported as $\mu\text{m}^2/\text{cm}^3$
Scanning mobility particle sizer	Electrical mobility diameter	Size resolved SMPS	Provides fast and accurate measurement of particle concentration and particle size distribution 2.5 nm - 1000 nm Concentration range from 1 to 107 particles/cm ³ Metrics: number size distribution
Fast mobility particle sizer / Engine exhaust particle sizer	Electrical mobility diameter / Unipolar diffusion charger	Size resolved FMPS EEPS	Provides fast and accurate measurement of particle concentration and particle size distribution: 5.6 nm - 560 nm Metrics: number size distribution
Electrical low pressure impactor	Unipolar diffusion charger	Size resolved ELPI	Real-time particle size distribution and concentration in the size range of 6nm - 10 μm Metrics: size distribution
Inertial spectrometer	Aerosol Time-of-Flight Mass Spectrometry	Size resolved	Provides accurate measurement of particle size distribution and chemical composition of individual particles Metrics: particle size distribution



4. RECOMMENDATIONS FOR EXPOSURE ASSESSMENT OF ENGINEERED NANOMATERIALS IN THE WORKPLACE

Step 3. Sampling

Before any measurement campaign, all instruments must be calibrated to assure high data quality. This may also include cleaning of the device, possibly by the vendor depending on the previous measurement campaign. Under a Tier 2 approach, the following steps are recommended:

1. Background measurements (far field)

1. Select the background measurement scenario most suitable for the situation.
2. Consider indoor versus outdoor variations as filtered inlet air will present a lower background than outdoor (ambient) air.

→ Recommendation: the time resolved total (number) concentration must be collected and documented for at least 45 minutes for both the assessment and the background.

2. Field Measurements: process/task specific measurements can be conducted. These measurements shall be conducted in the near field, understood as locations near the suspected emission source (0.5 to 1.5 m), and at the perimeters of process enclosures and extraction ventilation during operation. When possible, measurements in the same locations and processes but not involving ENMs should be conducted to differentiate between (a) manufactured nanomaterials emitted from the process and (b) incidental nanoparticles produced by the equipment.

In addition, measures at the particles breathing zone (PBZ) on an individual, defined as a 30 cm hemisphere around mouth and nose, are strongly recommended. Measurements in the PBZ require instruments that are small and lightweight, and may be accompanied by particle sampling for off-line analysis to obtain a more definitive proof for the presence or absence of ENMs. The sampling duration depends on the requirements for the subsequent analysis.

Prior to the activity to take place, some considerations must be taken into account:

- Minimum sampling time depends on the duration of the activity. At least 15 min of measurements are recommended for comparison of the measured exposure concentrations with an existing benchmark value.
- Zero check must be performed to the sensor of nanoparticles prior to measuring.
- Internal clock of the instrument must be checked and synchronise the current time to the precision down to seconds.
- Extra tubing to connect or redirect outlets to a focused point may be required. Avoid silicon tubing due to high risk of contamination of the instruments.

A Tier Three assessment involves:

- Collection of aerosols onto a filter membrane connected to a sampling pump or TEM grid within an electrostatic precipitator, with analysis by SEM/XRD and TEM/XRD respectively.
- Use of more complex measuring instruments e.g a scanning mobility particle sizer (SMPS) with the minimum particle measurement size possible for ultrafine particle concentration and count median diameter measurement.
- Using an Aerodynamic Particle Sizer (APS) or Optical Particle Sizer (OPS) for information on the size distribution of particles above 300nm in size (e.g. agglomerates)

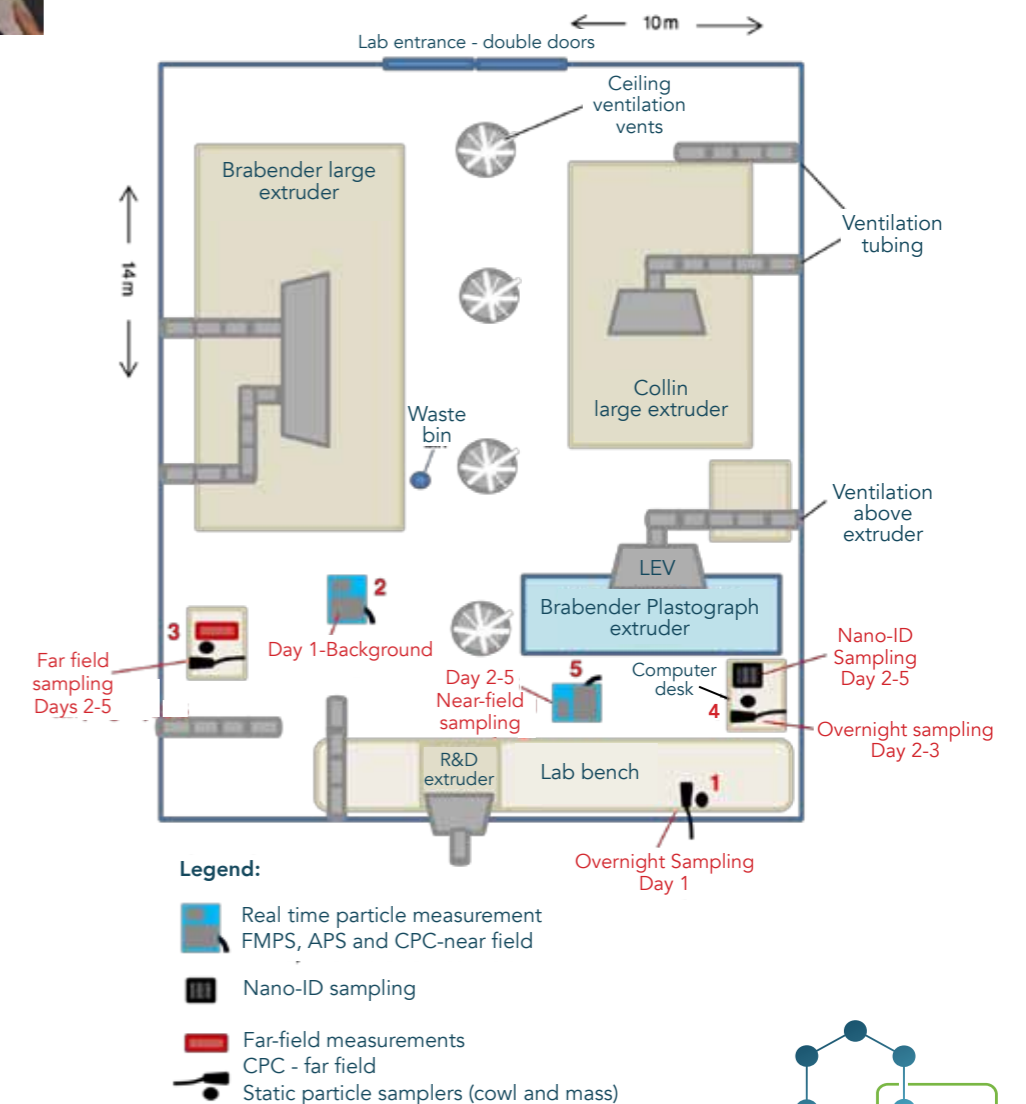
→ Where the results of Tier 3 assessment confirm the excursion in particle concentration is associated with the nanotechnology process, particle control strategies should be considered.

A schematic vision of an industrial facility is depicted in Figure 8 with the general depiction of recommended near-field sampling points.

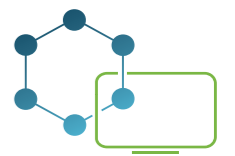
Figure 7. PBZ sampling approach



Figure 8. Schematic vision of an industrial facility and recommended locations for sampling instrumentations



Source: Nanosafepack project



4. RECOMMENDATIONS FOR EXPOSURE ASSESSMENT OF ENGINEERED NANOMATERIALS IN THE WORKPLACE

Step 4. Data processing and reporting

List of the minimum amount of data that exposure scientists should report when describing the results of an exposure assessment study (see Table 12).

The following data processing/analysis shall be conducted:

1. Describe the presence of other sources of nanoparticles, e.g. compressors, fork lifts, etc.
2. Plot the time-series data
3. Calculate the time-weighted average of the real-time particle number and mass concentration
4. Identify the presence of peak particle concentration values. Exclude peak particle values that are within \pm the manufacturer stated accuracy of the instrument of the timeweighted average of the real-time particle number and mass concentration.
5. Calculate the peak particle number and mass concentration values for the process operation.

The **NanoMONITOR station** provides real time information on a number of parameters. This information is depicted in Table 13.

The data from the sampling system must be analysed to obtain:

- In the case of cyclones, respirable/inhalable or thoracic mass gathered
- In the case of cascade impactors, mass of each stage.
- In the case of sampling filters, and in all other cases if possible, SEM/TEM microscopy to confirm the aggregation/agglomeration state of the ambient particles and their size/morphology, and EDX analysis to confirm their chemical composition and track their provenience.

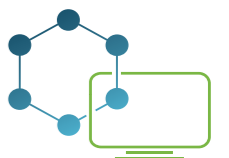
The **meta information** necessary to provide context to the data and allow interpretation is related with the atmospheric conditions, contributing processes and external conditions of the data acquisition. A comprehensive set of the meta-information required can be checked in the validation criteria tool "Reliability Assessment for Exposure Data.xlsm" developed under action A2, being accessible in the project web site.

Table 12. Minimum set of data to be reported in Exposure assessment studies

TIER 1 ASSESSMENT DATA	
Materials used – type, quantity, form	
Process operation	
Number and roles of workers associated with process	
Work patterns of workers including shift duration, work tasks and duration, work location	
Maintenance schedule and process	
Likely points of particle emission from the process	
Likely sources of incidental particle emission	
Current particle emission and exposure controls used such as enclosures, ventilation, and personal protective equipment	
Ventilation assessment including measurement of flow rates, air velocities and pressure	
TIER 2 ASSESSMENT	
Background and process particle number and mass concentration.	
Calculated averages of the measured particle number and mass concentration. Arithmetic mean is sufficient as the data is used for assessing relative concentrations.	
Time series plots of the data – identify median peak particle concentration values. Exclude particle values that are within \pm of the manufacturer stated inaccuracy for the instrument, i.e. peak values that are within \pm of the local particle reference value.	
Description of the peak particle number and mass concentrations relative to the local particle reference value.	
Identification of data assessment location - for example, at point of emission and in breathing zone of workers.	
TIER 3 ASSESSMENT	
The results of the off-line particle morphology and chemical composition analysis such as:	
Aerosols collected onto a filter membrane connected to a sampling pump or TEM grid within an electrostatic precipitator, with analysis SEM/XRD and TEM/XRD respectively.	
Sampling and analysis against a Workplace Exposure Standard, Recommended Exposure Limit, proposed workplace exposure limit, or benchmark exposure level have been established for the nanomaterial	
Detail of specific the sampling and analytical methods used.	
Data from other assessment methods such as scanning mobility particle sizer, including data on the setup parameters of the instruments.	

Table 13. Information provided by the NanoMONITOR station for the exposure assessment

SOURCE	MAGNITUDE	UNITS	I/O
Memory of monitor	ID station	Code nr	O
	Location	text	I
	GPS coordinates	gg:mm:ss	I/O
	Event recording	Sequential Code nr	O
	Comment	text	I
	Date	dd/mm/yyyy	O
	Time	hh:mm:ss	O
Environmental sensors	T environmental	°C	O
	P environmental	bar	O
	Relative humidity	%	O
Nanoparticle sensor	PNC	p/cc	O
	Geometric Mean Diameter	nm	O
	PMC	mg/m ³	O
	LDSA	um ² /ccm	O
	I filter	fA	O
	I Diff	fA	O
	Corona voltage	KV	O
Flow sensor	L/min	O	
Filter sampling	Flow channel 1	L/min	O
	Cycle number channel 1	Sequential nr	O
	Flow channel 2	L/min	O
	Cycle number channel 2	Sequential nr	O
	Flow channel 3	L/min	O
	Cycle number channel 3	Sequential nr	O



4. RECOMMENDATIONS FOR EXPOSURE ASSESSMENT OF ENGINEERED NANOMATERIALS IN THE WORKPLACE

Step 5. Risk Assessment

The criteria that determine the likelihood of exposure relies on the presence of ENM in the filters during activity, but not during the background, and the ratio between activity and background concentrations. These relations determining the probability of exposure are summarised in Table 14:

Although there is no standard, it is assumed that the concentration ratio activity/background must be greater than 1 to consider that there is release of NMs to the environment, and above a certain limit value (Cut-off value, CV) to consider that there is a potential risk of exposure.

For example, in the OECD ENV/JM/MONO (2016), it is considered that “if short term emissions or exposures exceeded three times the particle control value for time periods that add up to more than a total of 30 minutes per eight-hour working day there is significant exposure”, but depending on the ENM nature and toxicological properties, may be necessary to move this limit consequently.

Beside the above, there are a number of different types of particle control values that might be used for nanomaterial aerosols. To date, up to 20 studies that proposed in total 56 OEL values have been identified. Of these, two proposed a generic level for all MNMs, 14 proposed a generic OEL for a category of ENMs and 40 proposed an OEL for a specific nanomaterial.

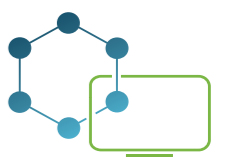
The following Table depicts proposed exposure levels for several groups of ENMs by international organizations such as the Institut für Arbeitsschutz der Deutschen Gesetzlichen Unfallversicherung (IFA), defined as nano reference values (NRV) by the the Social and Economic Council of the Netherlands (SER).

Table 14. Criteria for determining the probability of exposure through quantitative and qualitative measurements.

SEM/EDX		RATIO $C_{ACT}/C_{BG} > CV$	PROBABILITY OF EXPOSURE
NM BG	NM ACTIVITY		
X	✓	✓	Highly Probable
✓	✓	✓	Possible
X	✓	X	Not Excluding
✓	✓	X	
X	X	X	Low Probability / Negligible
X	X	✓	

Table 15. Proposed/ recommended exposure levels

CLASS	DESCRIPTION	DENSITY	NRV (8-hr TWA)	EXAMPLES
1	Rigid, biopersistent nanofibres for which effects similar to those of asbestos are not excluded	-	0.01 fibres/cm ³ (= 10,000 fibres/m ³)	SWCNT or MWCNT or metal oxide fibres for which asbestos? like effects are not excluded by manufacturer
2	Biopersistent granular nanomaterial in the range of 1 and 100 nm	> 6000 kg/m ³	20,000 particles/cm ³	Ag, Au, CeO ₂ , CoO, Fe, Fe _x O _y , La, Pb, Sb ₂ O ₅ , SnO ₂
3	Biopersistent granular and fibre form nanomaterials in the range of 1 and 100 nm	< 6000 kg/m ³	40,000 particles/cm ³	Al ₂ O ₃ , SiO ₂ , TiN, TiO ₂ , ZnO, nanoclay, Carbon Black, C60, dendrimers, polystyrene Nanofibres for which asbestos-like effects are excluded
4	Non-biopersistent granular nanomaterials in the range of 1 and 100 nm	-	Applicable OEL	e.g. fats, common salt (NaCl)



5. RECOMMENDATIONS FOR EXPOSURE ASSESSMENT OF ENGINEERED NANOMATERIALS IN THE ENVIRONMENT

5.1 Recommended measurement techniques and protocols for detecting, quantifying, and characterising of engineered nanomaterials in surface water, ground water and wastewater

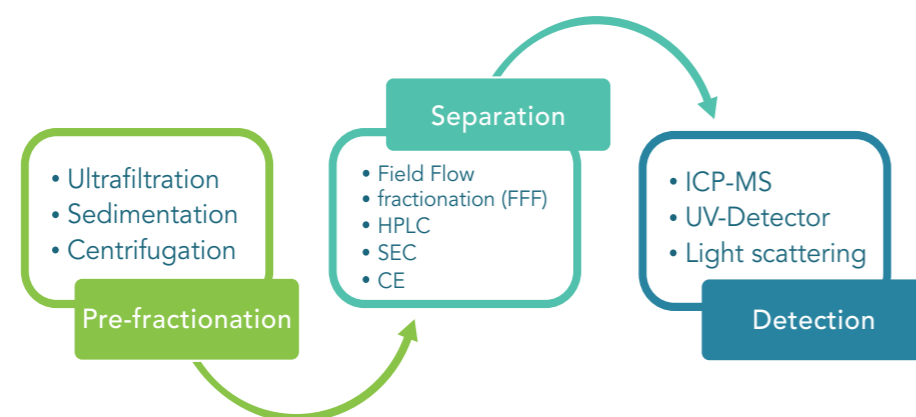
There is a lack of efficient and standardised methods for detecting, quantifying, and characterising engineered nanomaterials (ENMs) in surface water, ground water, and wastewater. Current scientific research has been focused on the determination of the presence of ENMs in different aquatic matrices (Wigginton et al., 2007; Simonet and Valcárcel, 2009; Scown et al., 2010). However there are several limitations that must be overcome: the three most relevant difficulties to be considered when sampling and analysing water ecosystems are: 1) to differentiate natural occurring nanomaterials and ENMs; 2) to detect these particles, as they are expected to be in the order of micro and nanograms, and 3) to analyse relevant nano-specific properties, including particle size, surface chemistry, or surface area, amongst other.

Moreover, due to the unstable nature of the ENMs when dispersed in water, especially in the case of colloidal nanoparticle dispersions, there is an urgent need to apply in situ analytical techniques, but these methods are rarely available. In addition, water samples are often collected in bottles that have been selected for minimum adsorption and contamination, e.g., plastics, especially fluoroplastics, for inorganic colloids or metal analysis and glass for analysis of organic trace constituents. In the specific case of ENMs, conventional sampling materials may have to be revised considering the composition and surface chemistry of common NMs, especially due to the use of organic coatings and surfactants. Similar concerns apply to all other materials to which the sample is being exposed (e.g. tubing, filter materials, pipettes, among others).

Due to the low stability of ENMs in water, several steps are currently recommended in the literature after sampling to support water sample analysis, including separation or pre-fractionation. In this regard, separation by size can provide important information on mass-based size distributions, determine compositional variations with size, and possibly distinguish ENMs from natural nanoparticles and naturally occurring colloids.

The most applicable techniques include capillary electrophoresis (CE), chromatography, and flow field fractionation (FFF), being this latest specially recommended when dealing with ENMs. FFF separates nanoparticles according to their particle size by their diffusion coefficients in a very thin open channel. The FFF needs to be coupled to a detector that responds to the nanoparticle number or mass concentration. Examples include: UV absorbance, light scattering, or elemental detectors such as ICP-MS. Figure 9 shows recommended steps to conduct the characterisation of ENMs/ENPs in water, groundwater and wastewater.

Figure 9. Recommended steps to conduct the characterisation of ENMs/ENPs in water



Regarding quantification and characterisation, there is still a high level of uncertainty due to the complex set of metrics that need to be measured, including particle size distribution, surface area, surface charge or aspect ratio, all of them relevant for evaluating exposure, behaviour and effects.

Imaging techniques are currently the most common methods for characterising the size and shape of ENMs, including scanning electron microscopy (SEM) or transmission electron microscopy (TEM), however, particle concentrations must be high (generally $>10^9$ mL⁻¹) to reliably find nanoparticles using any of the imaging methods.

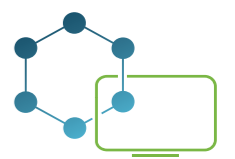
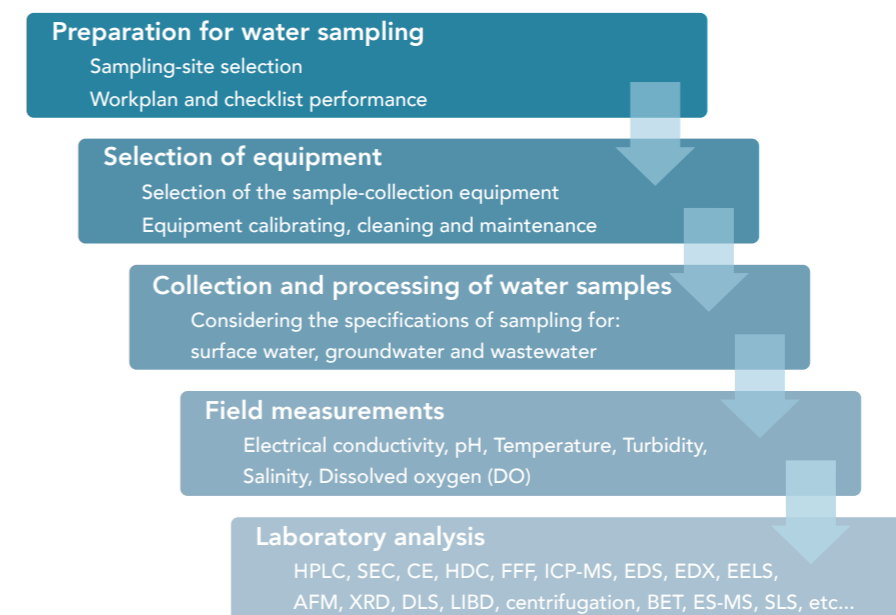
Representative nanoparticle size distributions can be obtained by a variety of light scattering methods. Dynamic light scattering (DLS) is the most prevalent light scattering characterisation tool, being applicable for ENM suspensions with narrow size distributions.

To quantify and characterise ENMs in natural media, element-selective detection methods are required. To date, inductively coupled plasma mass spectrometry (ICPMS) is by far the most common detection approach, because of its high sensitivity. However, most element-selective detection techniques, including ICPMS, cannot characterise particle size distribution, being commonly coupled with separation techniques such as field flow fractionation (FFF) or hydrodynamic chromatography (HDC). Both flow-FFF-ICPMS and HDC-ICPMS provide elemental information in addition to size distribution.

Besides the above, the selection of the detection and analytical techniques shall be based on the chemical nature and properties of the particles, considering metal or metal oxide based nanomaterials, and carbon-based nanomaterials. In this regard, the quantification of C60 fullerenes, graphene or carbon nanotubes, requires the use of specific techniques, including near infrared fluorescence spectroscopy (NIRF), High-performance liquid chromatography, or Raman spectroscopy.

Figure 10 shows schematically the recommended steps to follow in the sampling of water, groundwater and wastewater, as well as the considerations or the most important tasks that should be performed in each case.

Figure 10. Recommended steps for water systems sampling: the more relevant considerations and tasks (based on the Standard Operating Procedure for water, groundwater and wastewater sampling proposed in NanoMONITOR)



5. RECOMMENDATIONS FOR EXPOSURE ASSESSMENT OF ENGINEERED NANOMATERIALS IN THE ENVIRONMENT

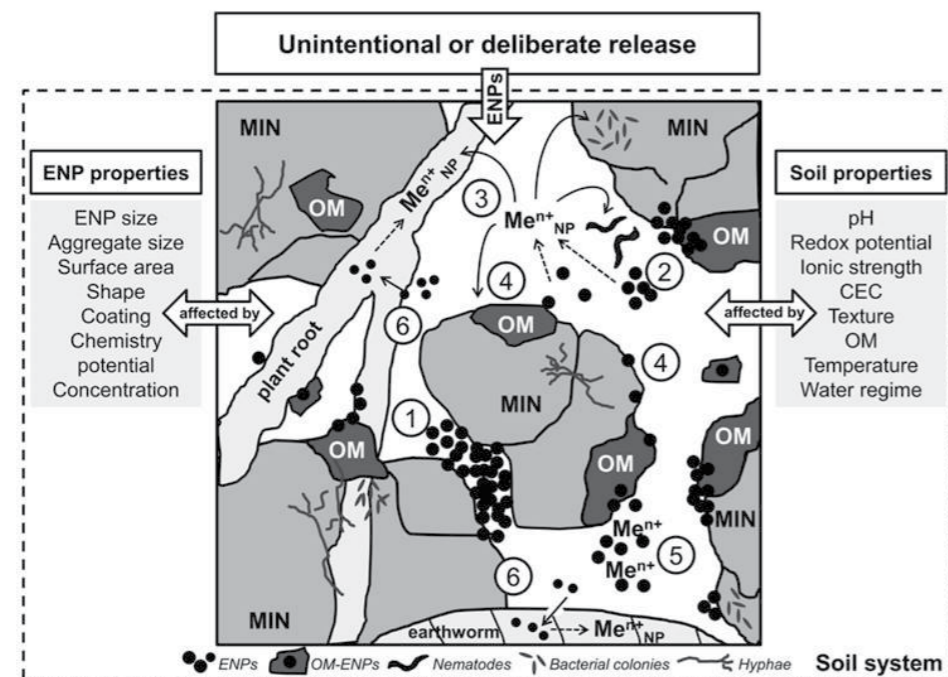
5.2 Recommended measurement techniques and protocols for detecting, quantifying, and characterising of ENMs in sediments, and soils

As in the previous case, there is a lack of an efficient and standardised methods for detecting, quantifying, and characterising ENMs in sediments and soils. The detection of ENMs in sediments and soils is a challenging task, hindered by the low concentrations of ENMs in the environment and comparably high background concentrations of particles composed of the important elements (Ti, Fe, Cu, Zn) in natural sediments and soil.

The largest obstacle to the detection and characterisation of ENMs in environmental samples is the large proportion of naturally occurring nanomaterials and colloids. Moreover, the detection of ENMs in the soil in the presence of natural colloids is difficult to perform. Natural nanoparticles in the soil (referred to as soil colloids) are difficult to separate and characterise (Noack et al., 2000; Gimbert et al., 2006, 2007). So, their reliable detection includes the separation of particles from soil solid phase (desorption) and their dispersion in a water suspension, which represents a serious analytical problem. It is also necessary to consider that soils contain both solid and liquid and gaseous phases and their chemical composition varies both horizontally and vertically.

Besides the above, another of the difficulties that affects the study of ENMs in soil is the complexity of the soil organomineral composition and the unpredictable dynamics of soil properties in time and space, which creates problems in the structural and chemical analysis of the soil. Figure 11 shows the complexity of the processes and factors that affect the behaviour and bioavailability of ENMs in a soil matrix.

Figure 11. Processes and factors affecting the behaviour and bioavailability of engineered nanoparticles in soils (CEC = cation exchange capacity; MIN = soil mineral particle; OM = organic matter) (Santiago-Martín et al., 2015).



1) Straining; 2) Aggregation/agglomeration; 3) Dissolution and release of free ionic metals (Me^{n+}_{NP}) from metal-based ENPs; 4) Sorption onto soil particles of ENPs or (Me^{n+}_{NP}); 5) Electrostatic stabilisation of ENPs with major cations (Me^{n+}) in the soil solution and in the solid phase; and 6) Uptake of ENPs by soil organisms

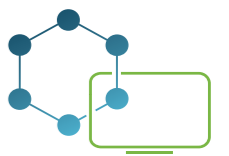
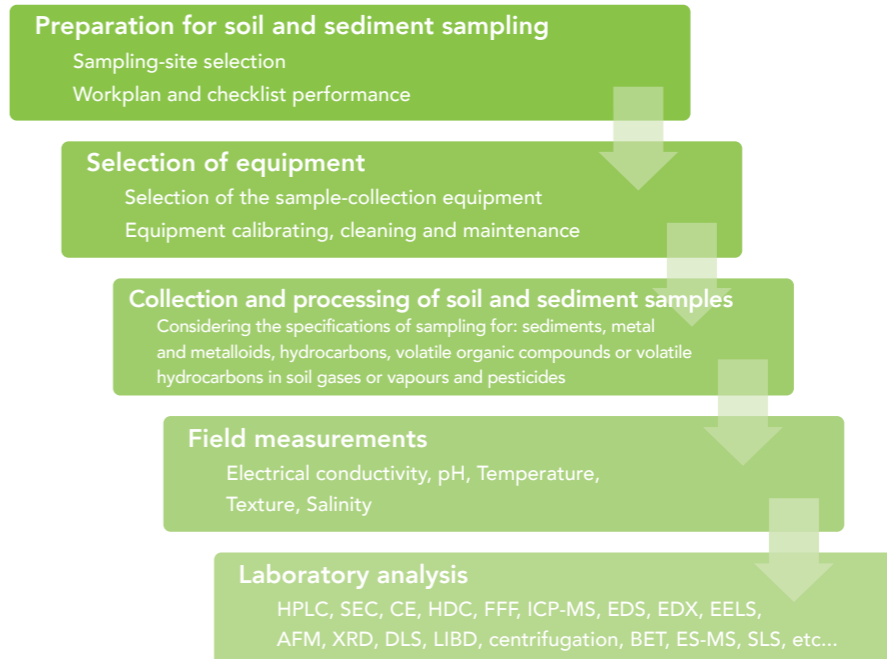
Under the current context, the detection, characterisation, and quantification of ENPs, especially in different matrices, are still challenging tasks and the analytical methods required to provide sufficiently reliable data are most often laborious, expensive, and/or demand specialised and trained operators. The identification, quantification and even further characterisation of the ENMs (e.g., in terms of particle size, composition, shape, or surface chemistry) requires the analysis on an individual particle basis. In this sense, time-resolved or single particle ICP-MS (spICP-MS) appears to be a particularly promising technique.

Inductively coupled plasma mass spectrometry (ICPMS) is by far the most common detection approach. However, most element-selective detection techniques, including ICPMS, cannot characterise particle size distribution, being commonly coupled with separation techniques such as field flow fractionation (FFF) or hydrodynamic chromatography (HDC) to provide additional information to discern the presence of ENMs from background natural nanomaterials.

Figure 12 shows schematically the recommended steps to follow in the sampling of sediments and soils considering current uncertainty due to the complexity of this compartment.

The selection of the detection and analytical techniques shall be based on the chemical nature and properties of the ENMs of concern, considering metal or metal oxide based nanomaterials, and carbon-based nanomaterials. As an example, the quantification of C60 fullerenes, graphene or carbon nanotubes, requires the use of specific techniques, including near infrared fluorescence spectroscopy (NIRF), High-performance liquid chromatography, or Raman spectroscopy.

Figure 12. Recommended steps for soil and sediment sampling: the more relevant considerations and tasks (based on the Standard Operating Procedure for soil and sediment sampling proposed in NanoMONITOR)



5. RECOMMENDATIONS FOR EXPOSURE ASSESSMENT OF ENGINEERED NANOMATERIALS IN THE ENVIRONMENT

5.3 Recommended measurement techniques and protocols for detecting, quantifying, and characterising airborne ENMs in urban areas

The objectives of this section are to provide users with:

- An integrated set of sampling protocols to quantify and/or identify airborne nanoparticles regardless of the source (natural nanoparticles or engineered nanomaterials from human activity).
- An understanding of the main principles to detect, analyse and quantify airborne nanoparticles, based in state of the art knowledge and instrumentation.

This section covers all the aspects for a correct sampling and analysis (in terms of identification of chemical components) of nanoparticles in air, including both, on-line and off-line techniques, as well as procedures for preservation and further processing of samples collected in a physical support.

Since its potential adverse effect on human health comes from the size of the particles, in this context it does not matter if they are natural or they are produced by human activity. We will use the term "nanoparticles" for both. It will refer to both, engineering materials or natural particulate matter, with basic structural units, grains, particles, fibers or other constituent components smaller than 100 nm in at least one dimension.

The sampling procedures described herein are applicable to the study of any type of nanoparticle.

There is a lack of specific legislation for particulate matter at this range (< 1 micron). Nevertheless, it is foreseeable that the new regulation (when it arrives) will be based on the experience and development of the regulated PM10 and PM2.5 included in the **DIRECTIVE 2008/50/EC** of the European Parliament and of the Council of 21 May 2008 on ambient air quality and cleaner air for Europe, which has been transposed to all member countries.

Considering this, we will now describe a first approximation of some procedures for measuring and characterising airborne NP.

5.3.1 Location of sampling points

Outdoor measurements of NP's concentrations are usually performed in order to characterise urban, suburban or industrial environments; while measurements in rural areas are usually considered as a background. Criteria exposed beneath have been extracted from the **DIRECTIVE 2008/50/EC**.

5.3.1.1 - Macroscale sitting of sampling points

Considering the protection of human health:

- Sampling points directed at the protection of human health shall be sited in such a way as to provide data on the following:
 - the areas within zones and agglomerations where the highest concentrations occur to which the population is likely to be directly or indirectly exposed for a period which is significant in relation to the averaging period of the limit value(s) (neither period(s) nor limit value(s) still regulated for nanoparticles)
 - levels in other areas within the zones and agglomerations which are representative of the exposure of the general population;
- Sampling points shall in general be sited in such a way as to avoid measuring very small micro-environments in their immediate vicinity, which means that a sampling point must be sited in such a way that the air sampled is representative of air quality for a street segment no less than 100 m length at traffic-orientated sites and at least 250 m × 250 m at industrial sites, where feasible;
- Urban background locations shall be located so that their pollution level is influenced by the integrated contribution from all sources upwind of the station. The pollution level should not be dominated by a single source unless such a situation is typical for a larger urban area. Those sampling points shall, as a general rule, be representative for several square kilometres;

- Where the objective is to assess rural background levels, the sampling point shall not be influenced by agglomerations or industrial sites in its vicinity, i.e. sites closer than five kilometres;
- Where contributions from industrial sources are to be assessed, at least one sampling point shall be installed downwind of the source in the nearest residential area. Where the background concentration is not known, an additional sampling point shall be situated within the main wind direction;
- Sampling points shall, where possible, also be representative of similar locations not in their immediate vicinity;
- Account shall be taken of the need to locate sampling points on islands where that is necessary for the protection of human health.

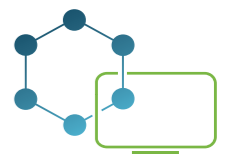
5.3.1.2 - Microscale sitting of sampling points

In so far as is practicable, the following shall apply:

- the flow around the inlet sampling probe shall be unrestricted (free in an arc of at least 270°) without any obstructions affecting the airflow in the vicinity of the sampler (normally some metres away from buildings, balconies, trees and other obstacles and at least 0,5 m from the nearest building in the case of sampling points representing air quality at the building line),
- in general, the inlet sampling point shall be between 1,5 m (the breathing zone) and 4 m above the ground. Higher positions (up to 8 m) may be necessary in some circumstances. Higher siting may also be appropriate if the station is representative of a large area,
- the inlet probe shall not be positioned in the immediate vicinity of sources in order to avoid the direct intake of emissions unmixed with ambient air,
- the sampler's exhaust outlet shall be positioned so that recirculation of exhaust air to the sampler inlet is avoided,
- for all pollutants, traffic-orientated sampling probes shall be at least 25 m from the edge of major junctions and no more than 10 m from the kerbside.

The following factors may also be taken into account:

- interfering sources
- security
- access
- availability of electrical power and telephone communications
- visibility of the site in relation to its surroundings
- safety of the public and operators
- the desirability of co-locating sampling points for different pollutants
- planning requirements.



5. RECOMMENDATIONS FOR EXPOSURE ASSESSMENT OF ENGINEERED NANOMATERIALS IN THE ENVIRONMENT

5.3.2 Work plan and checklist

5.3.2.1 Outdoor measurements

A work plan detailing and scheduling the activities to be conducted during the sampling campaign shall be developed by a responsible member of the organisation. Information about the company, organisation or institution, and the person in charge of the campaign must be reflected, as shown in next table.

A description of the measurement location must be included. It should take into account physical parameters (altitude, coordinates, meteorological conditions, etc.), as well as a characterisation of the area and activities developed on its surrounding (See Table 16). This general information will be useful independently the installation of on-line, off-line or both sampling techniques

It is also necessary to provide a well description about the instrumentation used to evaluate the concentration of NP's at the sampling point, as well as an explanation about how data have been recorded and/or managed by the device(s). So, information required by Table 16 should be incorporated.

Finally, if sample(s) is/are taking in a physical support (filter, cartridge or any other), a description about the sample(s) itself, as well as the process by which it has been taken, and the chain custody until it is analysed in a laboratory must be provided (see Table 17, 18 and 19). Sampling techniques (off-line measurements) can be used together with online instruments, but not necessarily.

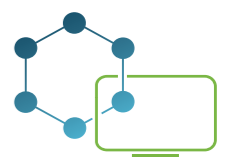
Table 16. Identification and contact

Project	
Institution/Organisation/Company	
Address	
Contact Person	
Phone Number	
Mail Address	
Summary of motivation/s to take such measurements (research, surveillance in desired locations, etc)	
Links to web pages including general information, reports or scientific papers related with the data	

Table 17. Characterisation of sampling location (Outdoors)

DESCRIPTION OF SAMPLING LOCATION	
General Information	Address
	City/Town
	Postal Code
Coordinates	Lat (00° 00' 00")
	Long (00° 00' 00")
Altitude	(m.a.s.l.)
Sampling Altitude	(m)
Is there representative meteorological data for the location?	Yes
	No
Is there any obstacle affecting the meteorological measurements (trees, buildings...)?	Yes
	No
Type of location	Unknown
	Urban
	Suburban
	Rural
Type of influence	Unknown
	Traffic
	Industrial
	Background
IF TYPE 'TRAFFIC'	
Closest distance to a traffic way	Unknown
	< 5 m
	5 – 25 m
	25 – 100 m
	100 m – 1 km
> 1 km	
Traffic density	Unknown
	Low
	Medium
	High

DESCRIPTION OF SAMPLING LOCATION	
IF TYPE 'INDUSTRIAL'	
Distance(s) to the main source(s)	Unknown
	< 100 m
	100 m – 1 km
	1 km – 10 km
>10 km	
Type of industrial activity	
Closest distance to a traffic way	Unknown
	< 5 m
	5 – 25 m
	25 – 100 m
	100 m – 1 km
> 1 km	



5. RECOMMENDATIONS FOR EXPOSURE ASSESSMENT OF ENGINEERED NANOMATERIALS IN THE ENVIRONMENT

Table 18 – Instrumentation and data management

DATA FILE(S) AND INSTRUMENT(S)	
Measurement period	Unknown
	1 hour or more
	Several days
	Several months
	1 year or more
Data integration period	Unknown
	10 min
	1 hour
	1 day
	The whole period
Number of variables included in the data files	1
	2
	3
	4
	5
	More than 5
Have the instruments followed a program for maintenance and calibration?	Yes
	No
Have data been checked and validated?	Unknown
	Yes
	No
Expected or measured nanomaterial	
Measured variable(s) and units	
Instrument 1	Brand
	Model
	Serial Number
Instrument 2	Brand
	Model
	Serial Number
Instrument 3	Brand
	Model
	Serial Number
Instrument 4	Brand
	Model
	Serial Number
Technique(s)	
Detection Limit(s)	
Resolution(s)	

DATA FILE(S) AND INSTRUMENT(S)	
Uncertainty(s)	Unknown
	0% -10%
	10% - 50%
	>50%
% Coverage (Valid measurements / Total measurements in a period)	Unknown
	0% - 25%
	25% - 50%
	50% - 75%
	>75%

Table 19 Sampling process and laboratory information

SAMPLING INFORMATION	
Sample ID	
Date	
Start sampling	
Physical support	Brand
	Type
	Composition
Sampling flow (units)	
Sampling period (time)	
Total sampled volume (units)	
Pump	Brand
	Serial Number
	Power
LABORATORY INFORMATION	
General Information	Laboratory name
	Address
	City/Country
	Samples receptor
Sample(s) reception date	
Number of samples	
Pre-treatment conducted (if needed)	
Preservation measures (if needed)	
Instruments / Techniques applied for the analysis	Instrument 1
	Instrument 2
	Instrument 3
	Instrument 4
Scheduled analysis in laboratory	
Observations	
Analyst	

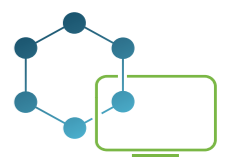
5.3.2.2 Indoor measurements

Similar to outdoor measurements, a work plan must be developed for indoor measurements, but the required information will be slightly different. Tables 1, 3 and 4 will be still valid and basically, the information that must be added is that related to the space indoor distribution and characterisation of the possible emission sources.

Table 20. Characterisation of sampling location (Indoors)

DESCRIPTION OF SAMPLING LOCATION (INDOOR)	
General information	Address
	City/Town
	Postal Code
Data integration period	Lat (00° 00' 00")
	Long (00° 00' 00")
Altitude	(m.a.s.l.)
Sampling altitude (from ground level if the location is an apartment)	(m)
Location of the instrument(s)	Living room
	Kitchen
	Bathroom
	Room 1
	Room 2
	Room 3
	Other
Number Of Windows In The Room	
Are they opened while sampling?	Yes
	No
Is there an extraction system in the room connected during sampling periods?	Yes
	No
Number of potential sources in the room	Unknown
	0
	1
	2
	More
Distance to source 1	Unknown
	< 1 m
	1 – 5 m
	5 – 10 m
	> 10 m

DESCRIPTION OF SAMPLING LOCATION (INDOOR)	
Distance to source 2	Unknown
	< 1 m
	1 – 5 m
	5 – 10 m
	> 10 m
Distance to source 3	Unknown
	< 1 m
	1 – 5 m
	5 – 10 m
	> 10 m
Sketch distribution	



5. RECOMMENDATIONS FOR EXPOSURE ASSESSMENT OF ENGINEERED NANOMATERIALS IN THE ENVIRONMENT

5.3.3 Measurement strategies and techniques

Directive 2008/50/CE defines the gravimetric measurement method as the reference method for assessment of concentrations of particulate matter (PM10 and PM2.5). In the same way, a reference method for sampling and measurement of particulate matter in the range nano can be expected, but it is not defined since there is not a regulation for nanoparticles yet.

5.3.3.1 In-situ (real time) measurements

A complete set of real-time devices is already available, including portable and non-portable instruments which monitor nanoparticles in quasi real-time to perform temporal and spatial analysis of particle concentrations and size distributions by applying different physical principles, fundamentally light scattering, electrostatic precipitation, vortex centrifugation, condensation and diffusion charges.

Particles smaller than about 50 nm do not interact strongly with electromagnetic radiation of optical or near optical wavelength, and so are not detected efficiently by light blocking or scattering. To overcome this range limitation, environmental nanoparticle number concentration measurements must employ another technique based on condensation, which effectively enlarge the particles to detectable sizes by condensing a low vapour pressure material (mainly butanol) onto the original particles from the gas phase (Morawska et al., 2009).

Particle size distribution in the submicrometer size range is generally measured with an instrument which includes a mobility particle sizer. Component systems feature an electrostatic classifier with a differential mobility analyser (DMA) that selects the size bins. Usually these instruments have another component, based on the condensation principle, who counts the number of particles in each bin. The sample first passes through a bipolar ion neutraliser which uses a radioactive source such as Kr-85 or Po-210 to ionise the particles into positive and negative ions and brings their charge level to a Fuch's equilibrium charge distribution (Wang et al., 2002).

The charged and neutral aerosols next enter the DMA where they are deflected by an electric field. Only particles within a narrow range of electrical mobility and, therefore size, are allowed to pass through an open slit into the counter. A variation, which improves a fast response, consists in placing a set of particle counting electrometers at multiple locations instead a unique condensation particle counter (Morawska et al., 2009).

Regarding health effects, total particle surface area is a parameter of interest since a good correlation has been found between some bad health conditions and particle surface area (Oberdörster et al., 2000; Brown et al., 2001). The active surface area is based on the integral collision cross section of the particles. The active surface of a single particle is approximately proportional to the inverse of the particle mobility. The total active surface can be calculated by integrating the measured mobility distribution or it can be measured directly via the adsorption of labelled species onto the particle (Burtscher et al., 2005). If the labelled species are radioactive atoms, then the method is called epiphaniometer, and if they are ions, then the method is called diffusion charger (Keskinen et al., 1992).

In a diffusion charging sensor, positive ions from a corona discharge diffuse onto the particles. After passing through the charging section of the instrument, the aerosol passes by an ion trap electrode, to which a low voltage is applied, and this removes the remaining ions. The charged particles are then precipitated onto an electrically insulated filter. The filter current yields the ion attachment rate (number of ions attached in unit time), which is proportional to the active surface of the particle ensemble (Konstandopoulos et al., 2004). The DC yields the same information as the epiphaniometer, but it is much faster and simpler to use, such that the response time is short enough to allow transient measurements. On the other hand, the DC is also significantly less sensitive, with a lower detection limit. This is because potential high particle charges have to be avoided, in order to avoid artifacts which may result from the repelling Coulomb force. The detection limit of around 1 $\mu\text{m}^2/\text{cm}^3$ is sufficient for direct measurement of emissions from sources, such as vehicles and ambient air measurement in urban areas (Wang et al., 2002).

Particle morphology and surface topography can be examined directly using Scanning Electron Microscopy (SEM). SEM uses a high energy electron beam to scan the surface of a sample resulting in the production of secondary electrons as well as characteristic X-Rays, as atoms in the sample surface are ionised. Back scattered beam electrons can also be detected. Each of these signals can be independently examined (Burtscher et al., 2005). When secondary electron imaging is used the surface of particle and provides depth of field as well as resolution down to a few nanometers. Hence SEM is very useful for examining the surface structure of nanoparticles and the nanostructure of larger particles (Morawska et al., 2009).

TEM can be used to image particles with much greater resolution than SEM, achieving lateral resolutions of fractions of 1 nm, however the technique is used for examining particle structure rather than surface topography. The sample is illuminated with a beam of high energy electrons and an image formed on film from the transmitted electrons (Morawska et al., 2009).

Table 21 shows an approximate size range of relevant methods applied in the characterization of nanoparticles.

5.3.3.2 Extractive (offline) measurements

A sample volume of the gas is removed from its environment and transported to a location where the measurement is made. The collection of air samples in adequate filter media is necessary to determine the chemical composition of the airborne nanoparticles, because particle classifiers are generally insensitive to particle source or composition.

Chemical characterisation of airborne nanoparticles is important, since, in addition to size particle chemical properties further influence the impacts of the particles on human health.

A common method to analyse a sample collected on a filter is to dissolve the material in water or another solvent, and then analyse the solution using regular analytical methods, including gas chromatography–mass spectrometry (GC-MS), ion chromatography (IC) and/or proton nuclear magnetic resonance (HNMR).

Although filters are inexpensive and easy to use, unfortunately, the very small mass of nanoparticles has posed a new challenge when using this sampling technology to determine their size-dependent chemical composition. As a result, when collecting size-classified nanoparticles for chemical analysis, impactors are the most frequently used devices. They can collect particles classified by aerodynamic diameter down to 10 nm, but ambient sampling process generally need to continue for days in order to achieve enough mass for laboratory analysis.

In order to shorten this sampling time, a USC Ultrafine Concentrator can be utilised to concentrate nanoparticles by a factor of 20-22 before sampling.

Advantages of impactors include their relatively high sampling rate, simplicity of operation and compatibility of sampling substrates with commonly used analytical methods. Bounce is a major disadvantage of using impactors to collect nanoparticles, as they rely on the particles sticking to the substrates when they impact, and after impaction, the dislodged particles become re-entrained in the air flow, such that they are then able to deposit on subsequent stages.

In addition to impaction, electrostatic precipitation is another effective sampling method for collecting nanoparticles. For example, the Nanometer Aerosol Sampler, consisting of a grounded cylindrical sampling chamber with an electrode at the bottom of the chamber, can be used to sample aerosols that have been conditioned and positively charged, like those from the output of a DMA, onto sample substrates for further analysis, such as SEM/TEM and GC-MS.

One limitation of these off-line methods is the poor time resolution associated with collecting a large enough sample for bulk analysis. Gas-phase partitioning after collection and contamination during handling are other issues that also need to be considered.

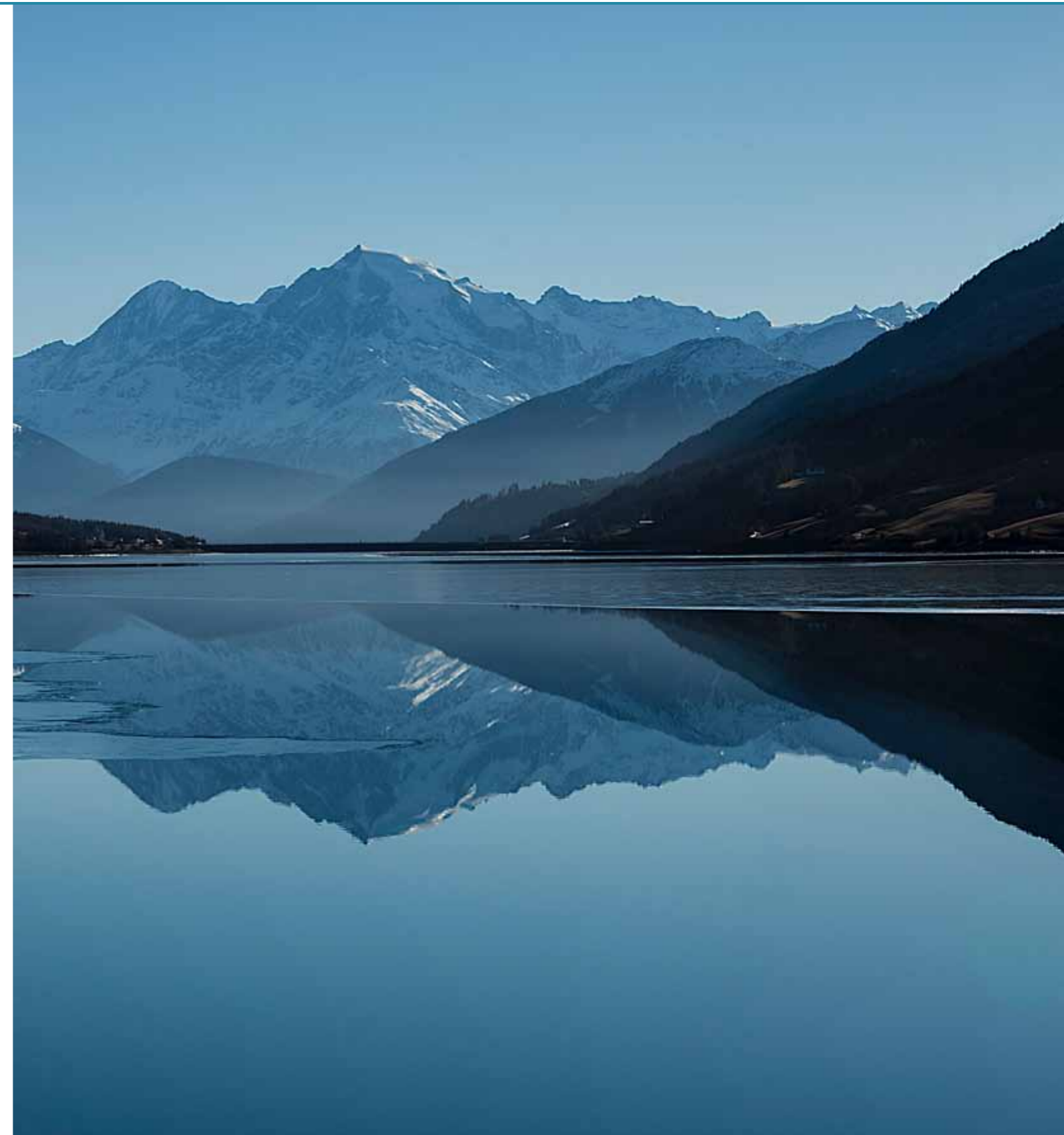
Finally, note that when developing an experimental design for nanoparticle monitoring under different conditions, several factors need to be taken into consideration, including the fact that:

1. Particle concentrations could be very high, exceeding the range of the instruments used and thus, requiring the application of a dilution system;
2. Variation in some operation parameters may lead to very rapid variations in source emissions;
3. Spatial variation of particle concentration could be very high, under certain circumstances exceeding an order of magnitude within a few meters of distance;
4. Temporal variation in particle concentration may reach several orders of magnitude in seconds;
5. Rapid formation of secondary nanoparticles may occur and the sampling process itself may actually affect this process;
6. Initial size of the newly formed nanoparticles could be below the size detection limit of the instrument used and therefore, they may pass undetected or they may be detected only if they grow to sufficiently large sizes;
7. Losses of particles could occur within the sampling system and sampling lines.

5. RECOMMENDATIONS FOR EXPOSURE ASSESSMENT OF ENGINEERED NANOMATERIALS IN THE ENVIRONMENT

Table 21. Specification of methods/ techniques to characterize airborne nanoparticles

TECHNIQUE / INSTRUMENT	MEASURED VARIABLE	CHARACTERISTICS OF THE SAMPLE	SENSITIVITY
Transmission Electron Microscopy (TEM)	Particle Size and Characterisation	< 1µg has to stable under an electron beam and high vacuum	< 1 nm
Scanning Transmission Electron Microscopy (STEM)			
High-Resolution TEM (HRTEM) Environmental TEM			
Scanning Electron Microscopy (SEM)	Particle Size and Characterisation	Sample must be conductive or sputter coated. Easier to prepare than TEM samples	< 1 nm
Environmental SEM			
Atomic Force Microscopy (AFM)	Particle Size and Characterisation	Samples must adhere to a substrate and be rigid and dispersed on the substrate. The appropriate substrate must be chosen. Air or liquid samples	1 nm – 8 µm
Scanning Mobility Particle Sizer (SMPS)	Particle Size and Characterisation	Aerosols. It can be a concentrated sample from 0 to 107 particles/cm ³	1 nm – 1 µm
Photon Correlation Spectroscopy (PCS)	Average Particle Size	Sample must be a very dilute suspension	1 nm – 10 µm
	Particle Size Distribution		
Differential Mobility Analyzer (DMA)	Particle Size Distribution	Aerosol	<3 nm – 1 µm
Condensation Particle Counter (CPC)	Particle Number Concentration	Aerosols with concentrations between 0 - 105 cm ⁻³ . T higher to 200°C possible	2.5nm – 3µm
X-Ray Diffraction (XRD)	Average Particle Size for a bulk sample	Larger crystalline samples (>1mg) required	<1nm
Aerosol Time of Flight Mass Spectroscopy	Particle Size	Aerosol	300 nm – 3 µm
	Particle Composition		
Aerosol Particle Mass Analyzer (APM)	Particle Mass Concentration	Aerosol sample with particle density approx. 1g/cm ³	15-580 nm
Aerodynamic Particle Sizer (APS)	Particle Size Distribution	Airborne solid and non volatile liquid samples. Concentrations between 0 – 104 cm ⁻³	370 nm – 20 µm
Fast Mobility Particle Sizer (FMPS)	Particle Size Distribution	Aerosol	5.6 -560 nm
Engine Exhaust Particle Sizer (EEPS)	Particle Size Distribution	Aerosol. Concentrations from 200 particles/cm ³ (corresponding to < 1µg/m ³)	5.6 -560 nm
Laser Aerosol Spectrometer (LAS)	Particle Number Concentration	Aerosol. Concentrations from 0 to 18000 particles/cm ³	90 nm-7.5 µg
Optical Particle Sizer (OPS)	Particle Size Distribution	Aerosol. Mass concentration from 0.001 to 275000 µg/m ³ and particle concentration limit up to 3000p/cm ³	10 nm - 10 µg
	Particle Number Concentration		
Portable Emission Measurement System for Particle Numbers (PEM S-PN)	Particle Number Concentration	Direct exhaust emission with a diluted measurement range of concentrations from 104 to 3x10 ⁸ particles/cm ³	10 – 700 nm
	Mean Particle Size		
	Lung-deposited Surface Area Concentration		
	Particle Mass Concentration		
Diffusion Charging Monitor	Mean Particle Size	Aerosol. Concentrations from 103 to 106 particles/cm ³	10 – 700 nm
	Lung-deposited Surface Area Concentration		
	Particle Mass Concentration		
Nanoparticle Surface Area Monitor (NSAM)	Lung-deposited Surface Area Concentration	Aerosol. Concentration between 0 and 104 µm ² /cm ³ being T between 0 and 38°C	20 nm - 1 µg
Epiphaniometer	Particle Number Concentration	Aerosol	70 nm - 5 µg
	Particle Size Distribution		
Ultrafine Particle Counter (UPC)	Particle Number Concentration	Aerosol. Concentrations from 0 to 5x10 ⁵ particles/cm ³	20 nm - 1 µg
Electrical Low Pressure Impactor (ELPI)	Particle Number Concentration	Aerosol	6 nm - 10 µg
	Particle Size Distribution		
	Particle Size Classification		



6. REGULATORY CHALLENGES

6.1 Regulatory framework

There are a large number of regulations and directives that may apply to users of chemicals across the European Union (EU). In addition, a number of member state countries have their own requirements for chemicals only applicable in that country. This chapter will briefly outline these legislations and will detail how engineered nanomaterials (ENMs) fit within them.

The legislative framework governing chemicals (often referred to as “substances”) is based upon the uses of the substance rather than the identity of the substance. A range of use-specific regulations and directives exist with their own requirements to allow a substance to be placed on the market for that purpose. However, these laws do not cover ALL the uses of a substance throughout its life-cycle, so Regulation 1907/2006 concerning Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) has been introduced to cover all other uses. This means that an entity placing a substance on the market for multiple uses may need to be compliant with more than one regulation.

Figure 13. Non-exhaustive diagram showing the relationship between EU legislation impacting upon substances.



The structure of EU legislation means that there are currently no nano-specific regulations across the EU. Instead, nanomaterials are controlled within the remit of different regulations depending on how they are used. A number of regulations do recognise that the physical, chemical, toxicological and eco-toxicological behaviour of ENMs can differ from other forms of the substance and indeed different nanoforms of the same substance might also present contracting behaviours, and therefore have specific requirements for nanoforms of a substance. The detailed requirements of the regulations will be given in section 6.2.

Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH)

Regulation (EC) No. 1907/2006 (European Commission, 2006)

REACH is intended to be an over-arching regulation that ensures that all uses of chemicals, not otherwise covered by a specific regulation, are performed safely within the EU. The regulation requires actions by entities throughout the supply chain of a substance. It not only covers the use of the pure substance but also mixtures containing the substances and articles manufactured using the substance.

A substance is defined as “...a chemical element and its compound in the natural state or obtained by any manufacturing process, including and additive necessary to preserve its stability and any impurity deriving from the process used...”. This means that a substance may contain more than one compound. A simple way of identifying whether a process is generating a substance or a mixture is to identify whether chemical bonds have been formed or broken during the process. If they have, the output of the process is a new substance. If no bonds have been broken or formed then a mixture is viewed to have been produced.

Nanomaterials are generally regarded as a form of a substance, rather than an entirely different substance. This means that the registration of a substance with nano-sized particles is done within the registration dossier of the parent substance, alongside bulk forms of the substance. Exemptions to this general rule have been the different carbon allotropes that have different crystalline structures and particle shapes (e.g. graphite (European Chemical Agency, n.d. a)), diamond (European Chemical Agency, n.d. b) Multi-walled Carbon Nanotubes (MWCNT) (European Chemical Agency, n.d. c) and Single-Walled Carbon Nanotubes (SWCNT) (European Chemical Agency, n.d. d) each have separate registration dossiers).



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Biocidal Product Regulation (BPR)

Regulation (EU) No. 528/2012 (European Commission, 2012)

The BPR is intended to cover all biocidal uses of a substance. A biocide is a substance that kill, deactivate, render harmless or prevent the action of a harmful organism. The BPR can be regarded as a two tier substance where a biocidal substance must be approved for use, then a product placed on the market must receive authorisation for its use. As part of both processes the hazard, exposure and risk assessments for the use of the active substance and the product are required. If the biocidal active substance falls within the definition of a nanomaterial, it must receive a separate substance approval to bulk forms of the substance.

Cosmetic Products Regulation

Regulation (EC) No. 1223/2009 (European Commission, 2009)

The Cosmetics directive requires that ingredients are shown to be safe for use within a cosmetic. The safety of ingredients used in cosmetic products is determined at EU level via evaluation by the Scientific Committee on Consumer Safety (SCCS). From these safety evaluations, positive and negative lists of substances that can or cannot be used in cosmetic products are created. It is the responsibility of those who supply cosmetic products to carry out product safety assessments on finished products. Substances that perform certain roles within the cosmetic and fall within the definition of a nanomaterial must be assessed separately to other forms of the same substance and the product must be labelled to clear show the ingredient that exists in a nanoform.

Food Contact Materials Regulation

Regulation (EC) No 1935/2004 (European Commission, 2004)

A series of regulations cover substances and materials that are intended to come into contact with food. If a substance is approved to be used within a food contact material it is placed on the Union List of Authorised Substances. If a substance on the Union List also exists as a nanomaterial, the nanomaterial is not regarded as being on the Union List and must be assessed separately. The risk assessment is focused on human health.

Medical Devices and In Vitro Diagnostic Medical Devices Regulations

Regulations (EU) 2017/745 (European Commission, 2017a) and Regulation (EU) 2017/746 (European Commission, 2017b)

Substances contained within a medical device must have a risk assessment. The complexity of the risk assessment depends on the likelihood of release of the substance from the device and the hazard of the substance. If the substance exists as a nanomaterial, a separate safety assessment is needed to the safety assessment of the bulk forms. Unless the nanomaterial is bound in a matrix so it cannot be released, the highest level of risk assessment is needed.

Provision of Food Information to Consumers Regulation

Regulation (EU) No 1169/2011 (European Commission, 2011)

The regulation states the information that should be provided to consumers via labelling, including ingredients, storage information and nutritional information. An ingredient that is intentionally manufactured as a nanomaterial must be labelled clearly stating that it is present in a nanoform.

Individual EU State Obligations

The basic tenets of the European Union requires that individual member states should not implement regulations where there is an existing regulation applicable across the EU. However, a number of states have implemented notification obligations on nanomaterial substances or products that contain nanomaterials.

- France (Ministry of Ecology and Sustainable Development, France, 2012)
 - Notification of substances, mixtures or articles with potential for release produced at over 100 g.
- Belgium (Kingdom Of Belgium Federal Public Service Health, Food Chain Safety And Environment, 2014)
 - Notification of nanomaterials substances produced on greater than 100 g.

- Denmark (Danish Environmental Protection Agency, 2014)
 - Notification of mixtures and articles where release is expected
 - Notification of any mixture or article where the nanomaterial is a carcinogen, mutagen or toxic to reproduction.
 - A number of uses are exempt from notification obligations
- Norway (Ministry of Labor and Social Affairs, Ministry of Justice and Emergency Affairs, Ministry of Climate and Environment, Norway, 2015)
 - Nanoforms should be reported separately within the chemical reporting scheme.
- Sweden (Kemikalieinspektionen, 2017)
 - Similar to French obligations.

6.2 Definition of nanomaterials and nanoforms

As the size of a particle decreases the surface area to volume ratio increases. Most reactions involving a solid occur on the surface of the solid, so as particle size decreases its reactivity per mass unit often increases (Khan, in press). In addition to their ability to access parts of the body that other forms cannot access, this potential increased reactivity have led to fears that the smallest particles of a substance might show significantly different toxicity than other forms (De Matteis and Rinaldi, 2018). These extremely small particles have been described by the term "nanomaterial". As nanomaterials have attracted regulatory attention, a formal definition of a nanomaterial has been required.

A draft definition of a nanomaterial has been in place for REACH since 2011 (European Commission, 2011b) and is as follows:

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 nm - 100 nm. In specific cases and where warranted by concerns for the environment, health, safety or competitiveness the number size distribution threshold of 50 % may be replaced by a threshold between 1 and 50 %. By derogation from the above, fullerenes, graphene flakes and single wall carbon nanotubes with one or more external dimensions below 1 nm should be considered as nanomaterials.

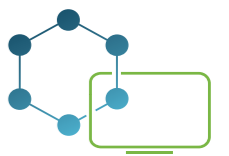
Revisions to this definition to give a formal definition is currently under consultation (European Commission, 2017c), but the number distribution of the magnitude of the shortest dimension of the primary particle is likely to remain as the key parameter used to define a nanomaterial. Other regulations in the EU base their definition of nanomaterials on this draft version, but may also include small variations to make the definition applicable to the individual regulation (Boverhof, 2015).

- Cosmetic Regulation specifies that a nanomaterial is insoluble or biopersistent.
- Cosmetics regulation and Food Information to Consumers regulation state that the nanomaterial must be intentionally made in the nanoform.
- The Food Information to Consumers regulation does not include a particle size distribution parameter in its definition but does allow particles of over 100 nm to fall under the definition if they demonstrate properties characteristic of the nanoscale.

Potential revisions to the REACH regulation may introduce the term "nanoform" into EU regulations. Although a formal definition for nanoform has not been proposed, the following definition has been used in documentation co-authored by European Commission organisations (European Chemicals Agency, 2016)

The term to distinguish forms of a substance that fulfil the EC Recommendation on the definition of the term 'nanomaterial' but differ with regard to size distributions, shape and/or surface chemistry.

It is not clear how the boundaries of different nanoforms should be defined or whether any form that slightly differs from existing forms would be regarded as a new nanoform.



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6.3 Risk assessment on a regulatory basis

Risk assessment is a key aspect of a number of regulations in the EU. The approach required for risk assessment is particularly clearly defined with REACH and BPR. This section will outline the overall risk assessment approach within REACH and the issues around how this can be applied to nanomaterials.

6.3.1 REACH

The REACH regulation places different obligations on different actors within the supply chain of a substance. It also places additional burdens on Substances of Very High Concern (SVHC) where the hazards associated with substance are particularly significant.

Registration

REACH applies the principle of “no data, no market” for substances that fall within the remit of the regulation. In practice this means that any entity manufacturing or importing a substance in the EU on over one tonne must have performed a hazard assessment on the substance and, if the hazard of the substance and the tonnage placed on the market requires it, they must also do an exposure and risk assessment for all uses of the substance that falls under REACH. In order to reduce animal testing and costs, REACH expects that the principle of “one substance, one registration” is applied. This means that one entity (the Lead Registrant) submits the hazard data and other entities needing to register the substance (Joint Registrants) pay to use this data in their own registration dossier. The joint registrant must be confident that the hazard data that they are purchasing access to is applicable to the substance they are placing on the market, meaning they must understand the composition of their substance. The information requirements required in the hazard assessment of a registrant depends on the total tonnage of the substance placed on the market by the registrant. In order to calculate total annual tonnage, the annual tonnages of different grades of the substance must be summed. The methodology required to derive the relevant hazard data is detailed in Annexes VII – X of REACH (European Commission, 2006) but some flexibility is afforded to the registrant to use methods that are applicable to the physical and chemical properties of the substance.

If a registrant registers a hazardous substance on a > 10 tonne per annum scale, they must include an exposure and risk assessment for all uses of the substance. The assessment should investigate all stages of the life-cycle of the substance, from manufacture until it becomes waste or it is destroyed (e.g. degradation or conversion to another substance during use) and the assessment is done as the substance exists during that use (e.g. a solid substance dissolved in a solvent should use a tool that can assess liquids). The exposure and risk assessments are used to identify suitable risk management measures to ensure the substance is used safely for workers, consumers, the general population and the environment. These are then summarised as Exposure Scenarios (ES) which must be added to the Safety Data Sheet (SDS) of the substance when the substance is supplied down the supply chain.

Issues pertinent to nanomaterials: Hazard Assessment

As REACH requires that hazard data submitted in a dossier is relevant to the substance placed on the market, it is important to know the chemical (e.g. purity), physical (e.g. crystal form) and particle parameters (e.g. size, shape, degree of agglomeration) of both the substance used to measure hazard data and the substance placed on the market. Although the wording of the regulations does not specifically require particle characterisation of solid forms of a substance currently, proposed revisions to the regulation may introduce this requirement to all registrants in 2020 (European Commission, 2017d). The small size, high aspect ratio and potential of higher biological activity of nanomaterials have all led to concerns that nanoforms of a substance would have a different toxicological profile to bulk form of the same substance. REACH requires that nanoforms of a substance are identified in the registration dossier and the registrant should decide whether a separate hazard, exposure and risk assessment for the nanomaterials is required.

Nanomaterials may have different physico-chemical behaviours to other forms, which means that some of the methodology used to derive the hazard endpoints should be adjusted to be applicable. Extensive guidance is given by ECHA to identify these endpoints (European Chemicals Agency, 2017a-d) but a summary is shown in Figure 14.

The hazard profile of a substance is usually regarded as an intrinsic property of a substance. However, because the hazard of a particle may be due to surface reactivity or the ability to access parts of the body, the hazard profile of different nanoforms of the same substance may be different. The nanoforms of a substance are able to inter convert through the life-cycle of the substance, meaning that the hazard of the substance may also change through its life-cycle. This should also be considered as part of the hazard assessment of the substance. It should be noted that this is not placing an additional regulatory burden on registrants of nanomaterials compared to other registrants as all registrants must consider the impact of degradation products as part of the risk assessment.

Figure 14. Examples of the physical, toxicological and eco-toxicological endpoints, whose methodology would need to be adjusted for nanomaterials from the approach recommended for other substances.

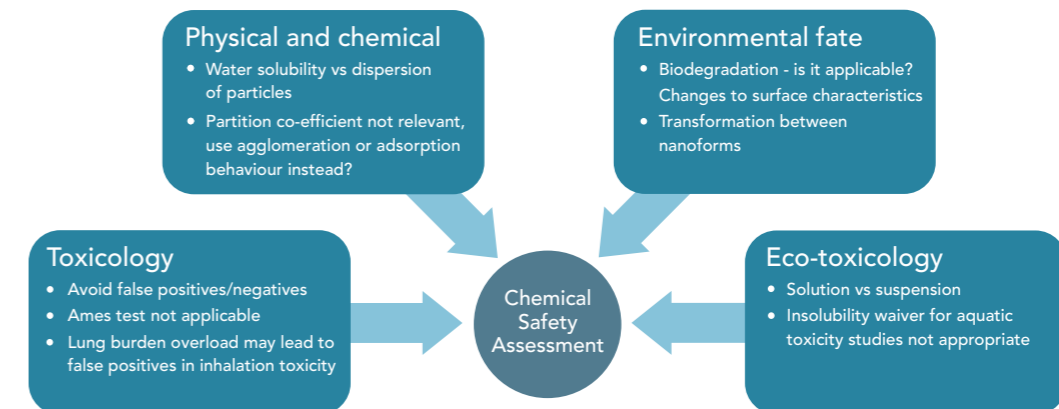
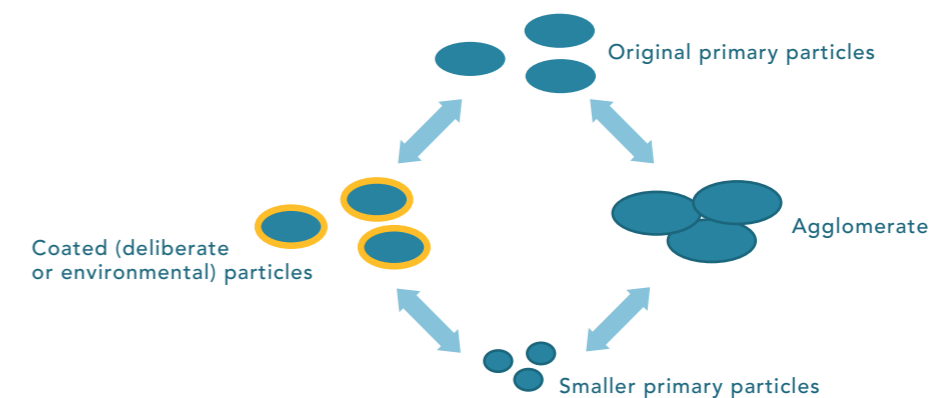


Figure 15. Interconvertibility of different nanoforms of the same substance



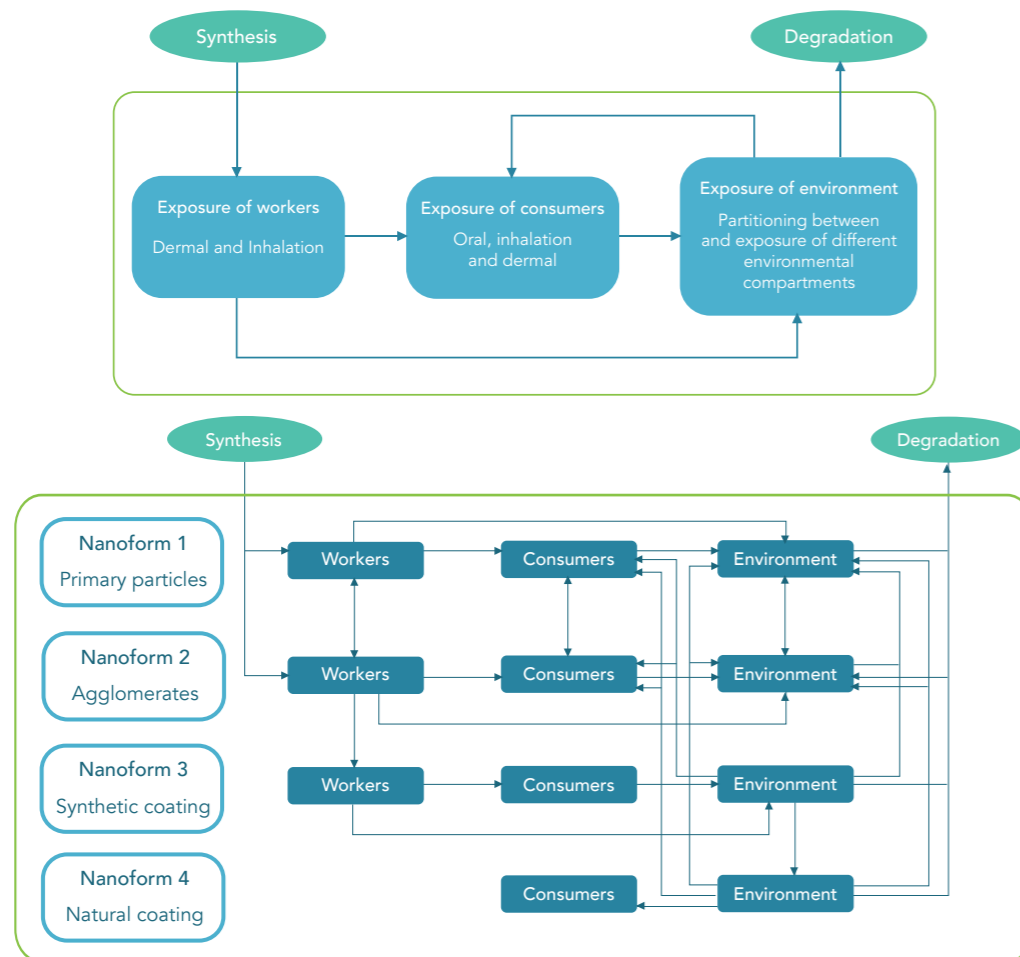
Issues pertinent to nanomaterials: Exposure Assessment

The first step of an exposure assessment under REACH is to identify all the relevant steps in the lifecycle of a substance, referred to as Exposure Scenarios (ES). Modelling software or direct measurement is used to estimate the exposure of target populations (workers, consumers, different environmental compartments, general population) to the substance. Exposure to populations that directly use a substance, such as workers or consumers, is generally based on the likelihood of the substance to be released during an activity (e.g. dusty substances have a greater exposure for inhalation than non-dusty forms). Exposure to the environment and of the general population is modelled using release amounts, how the substance partitions between different environmental compartments and how quickly the substance degrades.

For a simple organic substance, the substance enters the assessment in a pure form and leaves when it no longer exists, either because it is deliberately converted to another substance or it is degraded by biological or physico-chemical means (or becomes waste, but the Waste Directive (European Commission 2008) would then apply to the substance). The exposure assessment of a complex substance with multiple constituents is more complex, as different constituents might drive the toxicity of different route of exposure and partition differently in the environment (Figure 15). The ability of nanomaterials to interconvert between forms that might have different toxicological profiles makes the exposure assessment even more complex.

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Figure 15. Complexity of full life-cycle exposure assessment of different type of substance. Upper diagram: Mono-constituent organic substance. Lower diagram: Nanomaterial that can be found in different nanoforms.



The potential complexity of the life-cycle of a nanomaterial makes it important that a registrant and other users of nanomaterials (or nano-enabled products) to have a clear understanding of the behaviour of the nanomaterial as they use it. For example, what is the degree of agglomeration of the substance as it is used; can primary particles be released in biological and environmental systems from the form being used; are the particles coated during use, both intentional and environmental coatings. In order to complete a thorough risk assessment, the toxicology and environmental behaviour of each of these forms should be known.

Unfortunately, the research into the behaviour and hazards of nanomaterials when they are not in their pristine state is in its infancy. While there are some quantitative exposure models under development (e.g. Simplebox4Nano (Meesters, Koelmans, Quick, Hendriks and van de Meent, 2014)) that are undergoing validation by experimental measurements to give confidence in their use, many risk assessment models for workers and the environment are qualitative (Hristosov, 2016)

Obligations to downstream users

If a risk assessment must be included in a REACH registration dossier, there is an obligation to communicate the relevant information to allow safe use of the substance as an Exposure Scenario (ES) within the Safety Data Sheet of the substance. The ES should contain all the information to allow the recipient to apply adequate risk management measures or to assess whether risk management measures other than those stated are also adequate. A recipient may do this by demonstrating their measures have the overall effectiveness as the ones stated in the ES or they can physically measure the concentration of the substance in the workspace or environment (European Chemicals Agency, 2014). Using the same modelling software as the one used in the ES and entering their own measures would satisfy the former approach, but this requires that all

the parameters used in the ES calculation are included in the ES or the SDS. Directly measuring the substance requires a suitable sampling and analytical method. The difficulty to directly measure exposure to a substance would depend on whether there is a selective technique available and whether there is interference from other substances.

Issues pertinent to nanomaterials

Measuring exposure to nanomaterials to prove compliance with an ES has an increased degree of difficulty. As there are a likely to be a number of different possible nanoforms of the substance in a workplace or in the environment, the supplied ES might include information on exposure to only one form or to multiple forms. Therefore a sampling and analytical technique may need to be able to identify and quantify both chemical and physical aspects of the sampled material. It would then need to distinguish the ENM under investigation from other ENMs and natural NMs. This would not be a trivial undertaking, but it is hoped that the NanoMonitor project will provide equipment to approach this assessment.

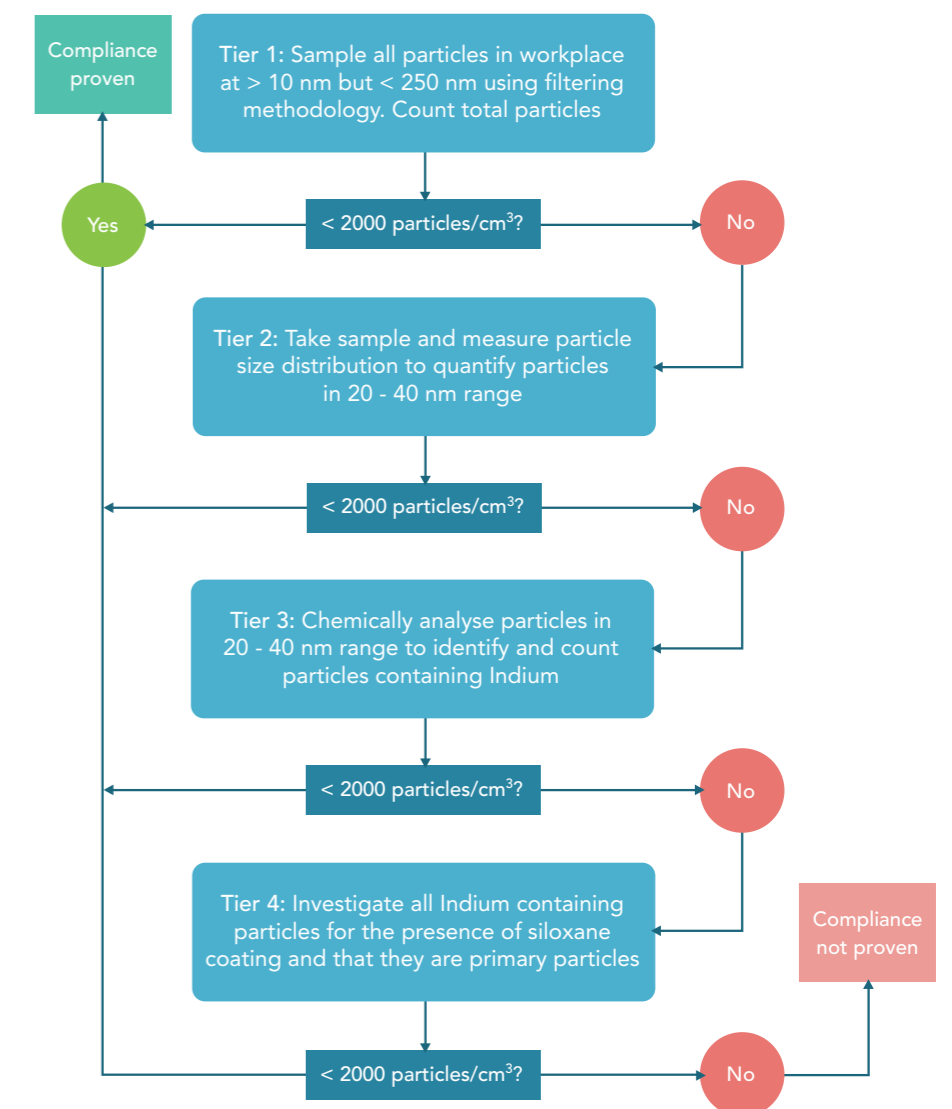
A tiered approach to sampling and analysis in the workplace and the environment would make proving compliance easier.

Example: The hazard assessment of an ENM containing indium showed that the most toxic nanoform was where the spherical primary particle in 20 – 40 nm range was coated with a siloxane. A safe exposure of this nanoform to the worker was calculated as 2000 particles per cm^3

A company using this ENM needs to prove compliance.

At each tier in the assessment, the company can decide whether it is more cost effective to move on to the more technically difficult next tier or to introduce risk management measures to prove compliance at that tier.

It would be possible to perform a chemical analysis for indium at tier 2 and the particle size assessment at tier 3. It would be up to the assessor to decide which approach would be most effective. For example, indium is rarely found in nature, so the chemical analysis might be most effective at discriminating ENMs from natural NMs. If the assessed NM was silicon based, the chemical analysis may not separate ENMs from natural NMs.



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Evaluation

Regulatory authorities can take further action to control risk associated with exposure to chemicals, but these actions are expected to be based on high quality scientific evidence. In order to use the REACH registration dossiers to assist in this process, the dossiers should be evaluated. The dossiers can be evaluated in two ways.

- **Dossier evaluation:** Inspects the dossier of an individual registrant to ensure all required elements are addressed in accordance with the regulations. For example, a dossier evaluation looks for missing information, studies performed by non-conforming methods or poor conclusions drawn from results.
- **Substance evaluation:** A substance suspected of displaying serious hazard and risks may be nominated for substance evaluation. The dossiers of all registrants are inspected to investigate whether a decisive conclusion can be drawn based on the information contained and whether additional studies should be mandated to strengthen any conclusions.

A number of substances known to be placed on the market as a nanomaterial have recently been evaluated. The European Chemical Agency has required additional information regarding identification of different nanoforms and specific risk assessment of these nanoforms. These requests have been appealed by the registrants and the Board of Appeal has found in favour of the appellants in a number of cases because the requests were not in line with the REACH regulations (European Chemicals Agency, 2017e). The proposed revisions to REACH are in direct response to these decisions.

Authorisation and restriction

If a substance is judged to present a significant hazard and/or risk, it may either have a restriction placed upon its use or it may require authorisation for its continued use. A restriction is placed on a specified use and may be a complete ban or a limit to the concentration the substance can be present in an article or mixture during that use. Restriction does not impact on any other use not named. If Authorisation is required, the substance or mixtures containing the substance cannot be used after a sunset date unless authorisation has been granted for that use. As of today, no substance often placed on the market as a nanomaterials or a nanoform of a substance has required authorisation or restriction.

6.3.2 Biocidal products regulation

The risk assessment required for active substance approval is similar to that required for REACH. However, there is not such extensive guidance for both hazard and exposure assessment for nanomaterials as there is with REACH, so it must be assumed that the REACH approach should apply. After active substance approval has been granted, any producer of a biocidal product containing the active substance should either purchase the substance from the entity holding the approval or apply for Article 95 listing within which they must prove technical equivalence.

Issues pertinent to nanomaterials:

Currently only one active substance in the nano-form has been approved (Synthetic Amorphous Silica) and this was because the approval was achieved through the Biocidal Products Directive (the pre-cursor to BPR) where no nano-specific requirements were included (Brinch, Hansen, Hartmann and Baun, 2016). In the absence of specific guidance within the BPR, it must be assumed that the detailed nano-specific guidelines for hazard, exposure and risk assessment of nanomaterials within REACH are also applicable to the BPR. In the absence of any nanomaterials reaching the end of the BPR approval process, it is not clear how the assessing bodies will approach the nano-specific sections of the risk assessment process.

If approval is given to an active substance present as a nanomaterial, it is unclear whether this approval can cover all other nanoforms of the same substance. The concept of nanoforms is not discussed in the regulatory text of either BPR or REACH, although revisions to REACH may change this in 2020. Associated guidance documents for REACH do discuss nanoforms but the term is not formally defined. The similar guidance documents for the BPR does not discuss nanoforms. If entities wish to place biocidal products in containing an active substance as a nanomaterial on the market, they will probably need to prove technical equivalence to the approved substance. Unfortunately, the guidance document published by ECHA on technical equivalence specifically states that it is not applicable to nanomaterials (European Chemicals Agency, 2017f) so how an entity is expected to prove technical equivalence is opaque. One aspect that must be achieved is that the risk to the environment cannot be greater than the substance granted approval, so monitoring of the environmental behaviour of new nanoforms during field trials of new substances would be useful in trying to prove technical equivalence.



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