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Review article

Nanomaterial exposures for worker, consumer and the general public

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ABSTRACT

Exposures to nanomaterials comprise the exposure to nano-objects, to nanostructured materials or nanocomposites being 'relatively' pristine at the place of production or 'aged' at later stages. This review presents the state of the art and current short-comings in nanomaterial exposure measurements and assessments with a strong regulatory focus. Overall, release and the study of release processes are central for understanding, modelling and minimising possible exposure, which holds true for worker, consumer and the general public exposure. Nanomaterial exposure assessment is furthest developed in the occupational field with different measurement devices, methods and significant data being already available. The biggest challenge here is harmonisation. Consumer exposure assessments are mainly based on combining release measurements and modelling using exposure scenarios since measurements on a regularly basis are not feasible. A tiered approach similar to the already established one for work places would be a significant improvement. There also is a strong need to further develop and harmonise methods. The least quantitative information is available for exposure of the general public via the environment. The measurement and analysis methods are limited and expensive in cases when manufactured nanomaterials have to be identified and quantified. Therefore, environmental nanomaterial concentrations are mostly modelled. Many parameters have to be estimated with uncertainties being often very high.

The summary of the current state of the art and challenges for nanomaterial exposure assessment for workers, consumers and of the public via the environment is performed to promote advancements in the different exposure assessment fields by facilitating cross-fertilization.

1. Introduction

Research on manufactured nanomaterial (MN) exposures of workers, consumers and via the environment of the general public has made major progress during the recent years indicated by an increase of publications from 18 in the year 2000, 1144 in 2010 to 3753 in 2016 (Table 1). Some of the health and safety research addressed was of fundamental scientific nature but also regulatory issues were addressed more and more as shown in Table 1. The term 'regulatory issues' in this review refers to laws, standards and general tools for regulation.

When looking at the regulatory areas addressed it can be noticed that most information and measurement data for engineered nanoparticle are currently available for worker exposure (e.g. Table 1). Much less is known about consumer exposure and such data have a higher uncertainty (e.g. Table 1). Exposure of the general population via the environment, as well as environmental exposure of the whole biota, is still the most challenging part due to low concentrations and limited analytical methods for engineered nanoparticles (Cornelis et al., 2014; Baalousha et al., 2016; Peijnenburg et al., 2015). The relative high number of publications listed in Table 1 for exposure via the environment is due to the high number of publications on ambient exposure to ultrafine particles, soot and other non-engineered nanoparticles. Only few articles found in the literature search for exposure via the environment were on engineered nanomaterials.

A review on nanomaterial exposure can be structured according to the field of regulations: occupational safety, consumer safety, safety of the general public and the environment. Another way of structuring the information could be according to the lifecycle of nanomaterials by discussing releases, emissions, transport processes, transformation and exposures for each life cycle stage. The focus of the latter one is from the perspective of a product whilst the first one focuses on safety and how regulation is set up. As this review intents to summarize relevant

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Table 1
Articles published per year

Key words*	Additional key words	2016	2010	2000
Nanoparticle, exposure, concentration		3753	1144	18
+ Regulatory or regulation		1174 (31%)	290 (25%)	4 (22%)[a]
	+ Work or worker or workplace	278	90	0
	+ Consumer	189	27	0
	+ Environment + Air or water or soil	547	120	2[b]

*www.scopus.com last searched 11th Sept. 2017.

[a] Note: 2001 was the first article on engineered nanoparticles related to regulation; this search include quite some literature on ultrafine and soot particles.

[b] Note: 2004 was the first article on engineered nanoparticles in the environment; this search include quite some literature on ultrafine and soot particles.

information to support regulation the information was structured according to fields of regulation. Information base for the review was focussed on reviewed publications, project reports and summaries funded by the EU, as well as literature reviews done in the framework of the European projects, especially NANoREG.

Exposure assessments rely on a basic knowledge of the measurement methods and strategies delivering the concentrations by which exposure can be determined. Other approaches are based on exposure scenarios or release processes. Modelling tools for occupational and consumer exposure are based on knowledge of release and emission. These specific models are becoming more and more available, and will also be discussed.

Exposures that could probably cause health concerns in the workplace where nanomaterials are produced or handled were the starting point of experimental research. Exposure measurements and assessments from industrial workplaces were first conducted at the end of the last and beginning of this century (Maynard et al., 2004 and Kuhlbusch et al., 2004). The basic questions in the first years approximately until 2008 were:

- How can we identify nanomaterials in air?
- How can we quantify nanomaterials in air?
- How can we differentiate manufactured from natural or incidentally generated nano-sized materials?

These questions were first investigated at workplaces for the reasons that (a) the kind of nanomaterial to identify and quantify was clearly defined, (b) the concentrations were the highest to be expected and hence likely of highest relevance and (c) well defined conditions were available facilitating the use of experimental measurement set-ups.

From 2004 onwards research about consumer exposures gained higher interest (Hoet et al., 2004 and Scopus search). The main focus was to be able to understand exposure and the possible effects of nanomaterials for consumers, and thus to deflect possible public concern. To achieve this, it was important to build on knowledge gained from workplaces, especially with regard to measurement methods. Several issues of concern related to exposure measurements and assessment beyond measurement methods were identified to be relevant in particular for consumer and environmental exposure.

Consumers can be potentially exposed to nanomaterials in products during different phases of the product lifecycle: production, processing, use phase, end-of-lifecycle. Assessment of consumer exposure to MN is complex, primarily because important information is often lacking. These relates to detailed information on the use of MN in consumer goods as well as to technical difficulties during measurement, in particular for liquid or solid products. Additionally, information on release during use and thus exposure is also not readily available.

Exposure via the environment is still the least developed area with respect to exposure measurements and assessment despite being addressed already in 2003 (Colvin, 2003). The reasons are simple but also demonstrate the current limitations in our knowledge. The first problem is the identification of the MN in the environment. In matrices like natural waters, particle agglomerates in ambient air, or soil it is unclear how a specific manufactured nanomaterial can clearly be identified and quantified due to the complexity of the matrix but also partially due to a high natural particle background. Measurement methods for these complex matrices with multiple influencing side factors are most demanding. Thus, any measurement method and strategy for assessing environmental exposure will need careful evaluation before it is ready to be used in regulatory settings.

The historical development of MN exposure assessments was also influenced by risk management options available for the protection of humans. Release and exposure conditions can be very well regulated and specific personal safety measures assured at workplaces. The possible uses of nanomaterial products by consumer are much broader and personal safety measures cannot be assured. Exposure assessments for the public have to consider all releases and environmental transformation processes. Hence they are presented and discussed in separate sections.

2. Release

Fragments of nanomaterials or nanoparticles have to be released before any exposure may occur. The conceptual approach of release as a prerequisite of exposure to nanomaterials started around 2008 (e.g. Müller and Nowack, 2008) discussing release into the environment for environmental exposure modelling. Subsequent discussions of nanomaterial safety research showed that the release processes are relevant in all exposure areas. Hence one key development in this field in recent years is summarised in the so-called Framework of Release (MARINA, 2014). Strictly speaking, the Framework of Release is a combination of existing concepts and tools linked in a framework to facilitate their regulatory development and use.

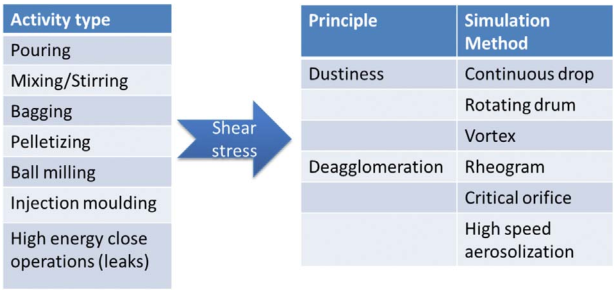
The basic concept is straight forward: A possible risk is only present if an exposure is possible. Release (separation from a larger unit) of nanomaterials or fragments of nanomaterials from powders, composites, suspensions or other nanomaterials is a prerequisite for any exposure. The step following release is the emission and transport of the released material into e.g. an airborne state which then can lead to an exposure of workers, consumers, public or the environment.

The framework of release encompasses four specific points:

The release processes: mechanical, thermal, chemical and mixed processes.

a) Test methods to simulate a process and to derive information on the effect of a given release process to a given material.
b) Linking a test method to an explicit activity or environmental process (see Table 2).

Table 2
Activity type and simulation methods: example for dustiness and de-agglomeration



Activity type
Pouring
Mixing/Stirring
Bagging
Pelletizing
Ball milling
Injection moulding
High energy close operations (leaks)

Principle	Simulation Method
Dustiness	Continuous drop
	Rotating drum
	Vortex
Deagglomeration	Rheogram
	Critical orifice
	High speed aerosolization

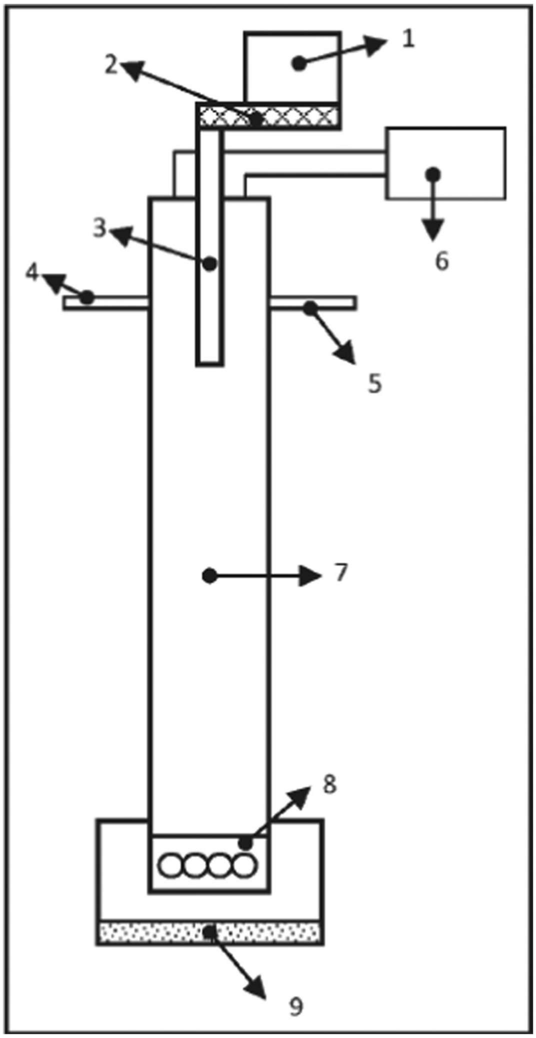


Fig. 1. Schematic continuous drop dustiness testing device: 1. Sample container, 2. Dispensing unit, 3. Drop pipe, 4. Sampling location SMPS, 5. Sampling location CPC, 6, Main stream pump, 7. elutriation air pipe, 8. Collection container for dropped material, 9. ULPA filter pack (adopted from Dahman and Monz, 2011).

c) Application of the information obtained in different settings such as exposure assessment, safe-by-design studies, abatement strategy development (see Fig. 1).

Release processes can be separated simply into mechanical (sanding, cutting etc.), thermal (incineration, heat stress, etc.) and chemical (dissolution of matrix material, etc.) processes. Also mixed processes exist like weathering (chemical and mechanical stress) or braking (mechanical shear forces and heat stress). Several test units were constructed to study releases by processes such as drilling, sawing, sanding, and cutting (Kuhlbusch and Kaminski, 2014; Froggett et al., 2014; Ding et al., 2017) and linked to relevant release scenarios. In some cases (sanding, weathering, drilling, de-agglomeration, dustiness) international round robin tests have been conducted or basic ISO standards are available.

Release tests can be used in different ways. Release data can be used in combination with modelling tools such as SprayExpo (www.baua.de), Stoffenmanager nano (Van Duuren-Stuurman et al., 2012; Bekker et al., 2016) or those described in MacCalman et al. (2016) for an exposure assessment. When discussing the tiered approach to assess exposure at workplaces (OECD, 2015), Tier 1 (Section 3.5) assesses the likelihood of exposure. If materials and processes are known, the assessment can be based on release processes.

One of the most advanced release test methods is that of dustiness (Fig. 1). Dustiness can be seen as an extrinsic property which characterizes a nanomaterial (Gao and Lowry, 2018). The aim of such test method is to predict the amount of release of fine particles during handling of the powders such as bag filling. The test was originally developed for coarser particles but has recently been adapted for nanoparticle release testing (EN 15051).

Several test methods have to be distinguished when discussing dustiness tests and the release of nanomaterials from powders. The continuous drop method according to EN 15051 (Fig. 3) that is similar to the rotating drum method (also EN 15051) simulates weak forces leading to powder disintegration and release of airborne particles. These forces acting on the agglomerated nanoparticles are called drag forces. In the case of EN 15051 these drag forces are related to the particle dropping/sedimentation speed (Ding et al., 2015). In some workplace exposure scenarios, the forces applied to agglomerated nanopowders are stronger than the drag forces, e.g. when there is a leakage during production, or active mixing of nano-powders with other materials, or in extruders. Further refinements have been made and reported by Stahlmecke et al. (2009) and by Ding et al. (2016) considering the stronger drag also called shear forces by forcing the aerosol through a nozzle, thus increasing the force acting on the agglomerates and then determining the extent of de-agglomeration. Ding et al. (2016) could demonstrate that de-agglomeration is directly dependent on the forces applied to the agglomerates. A comparison of different de-agglomeration test units showed that further development to achieve better agreements are still needed (Ding et al., 2017).

Taking the example of dustiness and de-agglomeration of powders, several activity types can be differentiated leading to different shear force levels (Table 2). Shear forces can be low, for example when the powder drops down onto the floor or can be very high during injection moulding. Therefore, tests simulating the different shear forces are needed and have been developed.

With these tests and applying them to different materials, the range of release probabilities can be determined, and used in exposure assessment studies, life cycle assessments, including environmental release, or safer-by-design product development (Fig. 2). A recent review on release tests and a first library can be found in Koivisto et al. (2017).

2.1. Release from commercial products

Product-use related aging and transformation processes affect MN during the use phase of their life cycle and hence influence consumer exposure. Thus, exposure assessment of consumers (or the general public via the environment) has to deal with aging and transformation processes altering the characteristics, the exposure potential and possibly also the hazard potential of the material. Only recently, the need to obtain data on MN release during the product use phase has been recognised. However, this data is essential for characterizing and quantifying consumer exposure. Methods for the identification of aging and transformation processes, as well as release assessment are reviewed in this section.

Experimental case studies documented in literature provide solid evidence for the release of MN from products. There are, however, major limitations regarding the analytical techniques available to quantify and characterize the particles released. The recently published review by Mackevica et al. (2016), evaluated to what extent information and data in the literature can be used to perform consumer exposure assessment according to REACH requirements. Less than half of the 76 reviewed studies report their findings in a usable format. Most of them do not include particle characterization. The main conclusion is that most of the available release studies do not reflect realistic conditions and are not able to illustrate actual characteristics of the released particles and their emissions.

Different aging and transformation processes through the lifecycle of nano-enhanced products were reviewed in Mitrano et al. (2015). This

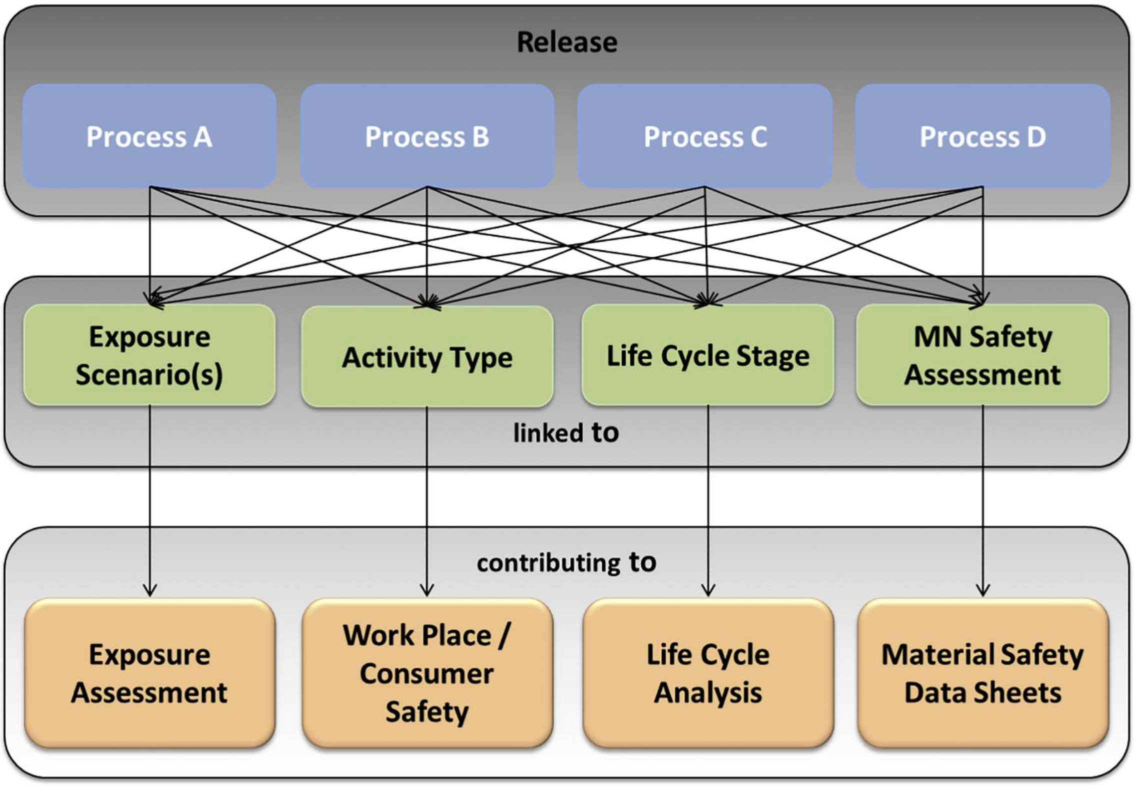


Fig. 2. Various uses of release test methods for safe use of nanomaterials

has been done for various consumer product categories and for various MN (Table 6).

The methods described in the two review papers (Mackevica et al., 2016; Mitrano et al., 2015) help to derive better estimates of actual exposure and risks for both consumer and the environment. They give a concise description of the various methods and approaches for the processes of aging and transformation. The methods seem reliable and are of high relevance for regulatory purposes. But further evaluation and round robin tests to assess the robustness are needed.

Within the limits of a typical experimental set-up it is very difficult to obtain enough released material for a proper characterization and more so for toxicological testing. Nowack et al. (2016) developed an approach to obtain sufficient quantities of released materials (fragmented products (FP), weathered fragmented products (WFP), sieved fragmented products (SFP)) to study MN in different life-cycle stages including end-of-life. In this way, the released material can be compared to the pristine materials for which a significant amount of data being already available. More processes to produce FP and WFP are needed because some products may be exposed to different stress processes during the life cycle.

However, the methods discussed in the papers of Mackevica et al. (2016) and Heggelund et al. (2016) refer to case studies that represent a limited number of MNs, products, and geographic regions. However, it currently remains unclear how well such studies represent real-world scenarios. For instance, the experimental set ups are often far from real-life conditions, which renders the data difficult to interpret in the context of environmental and consumer risk assessment.

With respect to protocols for aging simulation and detection of released fragments the methods are in general well-established and well-described with sufficient detail. Wohlleben et al. (2014) report the critical parameters of nanoparticle release by means of a pilot inter-laboratory comparison using a polyamide based composite containing 4% (m/m) of SiO_2 nanoparticles with a focus on the validity range of the aging and release protocols. After comparison of several different degradation protocols and several methods for identification, quantification and characterization of the bulk material and released fragments, a combined protocol was proposed. Other studies from Wohlleben et al. (2016a, 2016b) and Wohlleben and Neubauer (2016) describe a harmonised NanoRelease protocol that has been developed by different institutions (US-EPA, BASF, LEITAT, Can-NRC) testing different MNs, product groups and parameters. In these protocols, in which ISO-standardized aging equipment has been used as well as generally available sampling and analysis equipment, different release processes (i.e. processes as a consequence of weathering and aging), have been tested. In conclusion aging processes are more important for the MN release than the specific characteristics of the matrix and the MN itself. Aging conditions seem to be critical for release rates, but not for release characteristics. Therefore, to achieve reproducible and standardized release rates, highly controlled aging conditions are most critical. Furthermore, only synergistic stresses induce a significant amount of MN release (Wohlleben et al., 2016b). Since the results are comparable between laboratories, the tested protocols seem to be reliable. In the review of Koivisto et al. (2017) quantitative release of MN from different consumer products has been defined and calculated (release fragments of 60 studies) in order to develop a library that contains release data from nano-enabled products in a harmonised form (Koivisto et al., 2017). Such data is urgently needed for the improvement of modelling based assessments of consumer exposure.

3. Workplace exposure - measurement and assessment methods

Workplace exposure can occur in areas where nanomaterials are produced, handled and processed or those where nano-enabled products are used by professionals. A list of workplaces in the regulatory framework of REACH is e.g. given by ECHA (2016b). For this review, all workplace-related exposures to “as-manufactured” nanomaterials, and resulting releases from sites of production or incorporation into matrices like air or liquids are of interest. Exposure scenarios e.g. in REACH registrations typically contain information on the following points: the procedures involved during synthesis; use or disposal of the

Table 3
Exemplary ISO and CEN standards and guidance specifically addressing nano.

DIN EN 16897: 2015	Workplace exposure – Characterization of ultrafine aerosols/nano-aerosols – Determination of number concentration using condensation particle counters;
DIN EN 16966: 2016	Workplace exposure – Metrics to be used for the measurements of exposure to inhaled nanoparticles (nano-objects and nanostructured materials) such as mass concentration, number concentration and surface area concentration;
DIN CEN ISO/TS 12025: 2012	Nanomaterials – Quantification of nano-object release from powders by generation of aerosols;
ISO DTS 12901: 2012	Nanotechnologies – Guide to safe handling and disposal of manufactured nanomaterials – Part 1: Guide to safe handling and disposal of manufactured nanomaterials;
ISO TR 12885: 2008	Nanotechnologies - Health and safety practices in occupational settings relevant to nanotechnologies;
DIN EN ISO 28439: 2011	Workplace atmospheres – Characterization of ultrafine aerosols/nano-aerosols – Determination of the size distribution and number concentration using differential electrical mobility analysing systems;
ISO/TR 27628: 2007	Workplace atmospheres – Ultrafine, nanoparticle and nano-structured aerosols – Inhalation exposure characterization and assessment;

MNs; the associated operational conditions of use; the risk management measures and waste treatment techniques which are necessary for safe use; and information about the exposure estimation and the models used for this purpose. Thus exposure scenarios under REACH also include elements of risk assessment.

The inhalation exposure route is currently regarded as the main route of concern in particular for workers. Therefore, measurement techniques and strategies are most advanced for airborne nano-objects. The OECD suggests a tiered approach to measure and assess exposures to airborne emissions in workplaces (OECD, 2015). Methods to determine exposure include measurements as well as models like Stoffenmanager nano (TNO, 2012; Väänänen et al., 2014) to estimate exposures. Most of the current models used for regulatory purposes include stochastic approaches. Mathematical models based on physical and chemical principles may be more precise but need much more information and a higher level of education by the user. Anyhow, also for all modelling it has to be noted that the application and interpretation of the modelling results need to be assessed by experts since no "standard" exposure scenarios or libraries exist for the models.

Several measurement and modelling methods needed for an exposure assessment in workplaces are currently available e.g. at ISO (e.g. Table 3) and the OECD. OECD test guidelines are quite extensive and comprise the areas of physical and chemical characterization, environmental behaviour, environmental effects, exposure assessment and effects on human health (http://www.oecd.org/science/nanosafety/).

Some OECD test guidelines and guidance documents for physico-chemical properties, degradation, e.g. in the environment, and accumulation (OECD, 2015), address exposure endpoints. Where appropriate, these test guidelines (TG) and guidance should be used. Within the OECD Working Party on Manufacturing Nanomaterials (WPMN) the OECD test guidelines were checked for their applicability for nanomaterials. Results of this are e.g. published in reports in the Series on the Safety of Manufactured Nanomaterials.[1] Currently, some of these guidelines and guidance documents are updated and adapted for application for nanomaterials.

It should be noted that measurement methods and strategies in this section are solely discussed from the perspective of exposure assessment at workplaces and not as an integral part of material characterization per se. However, that some of the methods discussed here may also be useful for such purposes.

Due to the focus given on airborne exposure in the workplace, only those methods relevant for airborne particles are explained and discussed below. It may be concluded that measurement methods for the assessment of dermal and oral exposure are less well developed compared to those for airborne nanomaterials.

3.1. Measurement devices

Exposure related measurements of nanomaterials (including agglomerates and aggregates) have so far been conducted solely in exploratory research related projects (e. g. Kuhlbusch et al., 2011; Kaminski et al., 2015; Plitzko et al., 2013, Pietroiusti and Magrini, 2014). There is currently no legally binding regulation worldwide defining how and with which instruments exposure measurements to engineered nanomaterial have to be conducted to our knowledge. Workplace exposure measurements of e.g. the alveolar particle size fraction (particle diameters $< 4\,\mu m$ for worker) are usually based on personal measurements. Early workplace measurements to nanoparticles and their agglomerates were based solely on stationary measurements whilst recent developments now also enable personal exposure measurements in breathing zones (e.g. Asbach et al., 2016; Azong-Wara et al., 2013).

Several recent publications including ECHA (2016b), OECD (2014, 2016), Linsinger et al. (2012) present overviews of measurement methods indicating their strength and applicability for different tasks (Table 4). Several research papers also give information on the data quality, comparability and reproducibility of the different measurement methods (e.g. Asbach et al., 2012; Kaminski et al., 2013; Zimmerman et al. 2014) so that a first overview of measurement methods and their applicability is available.

Data quality as well as data interpretation is quite variable and results are often not comparable to each other due to e. g. use of different methods, metrics and particle size ranges. Nevertheless, measurement strategies and methods have been employed in research, in combination with a concise data interpretation, showing that data can be obtained fulfilling the requirements on reliability and relevance for human exposure assessment in the framework of regulatory risk assessment (e. g. Kaminski et al., 2013; Asbach et al., 2012; Zimmerman et al. 2014; Asbach et al., 2016). Instrument comparability in the field was found to be in the range of 50% for online particle number and surface area measurement devices if the same particle size ranges were investigated. Overall, there are very few investigations on measurement device comparability, reproducibility, or comparisons of measurement strategies[2] (Table 5). Those showed a general comparability. However, currently no definite statements on the robustness of results can be made before larger round robin tests have been conducted.

Different measurement methods can be identified as suitable, depending on the measurement targets. Measurements of the spatial distribution to identify possible spots of high exposure concentrations, particle sources or general monitoring can best be measured by mobile online monitors such as those based on diffusive particle charging and electrical detection. The latter types of instruments are quite robust,

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[1] http://www.oecd.org/env/ehs/nanosafety/publications-series-safety-manufactured-nanomaterials.htm

[2] Measurement methods relate to a measurement device whilst measurement strategies include the way devices are employed in the field and how data have to be treated to obtain results.

Table 4
A brief list of available measurement principles for airborne nanoparticles and their size distribution: applicable particle size range and measured metric.

Measurement principles	Example of available instruments	Applicable size range	Metric measured	Reference
Electrical mobility	SMPS, DMPS, FMPS	1–1000 nm	NC, PSD	Asbach et al., 2012
Cascade impaction	ELPI	1 nm–10 µm	NC, PSD, MSD	Leskinen et al., 2012
Diffusion charging	NSAM, nanoChek, nanoTracer, minidisC	20 nm–400 nm	LDSA, NC	Kaminski et al., 2013
Light scattering	OPS, OPC	200 nm–20 µm	NC, PSD	Black et al., 1996
Laser light scattering		50 nm–1 mm	NC, PSD	Black et al., 1996
Condensation	CPC	1–1000 nm	NC	Mordas et al., 2005
Electron microscopy*	TEM, SEM	0,1 nm–1 mm	NC, PSD	e.g. ISO TS 11888: 2011

NC Number concentration; PSD Particle size distribution; MSD Mass size distribution; LDSA Lung deposited surface area; SMPS Scanning mobility particle sizer; DMPS Differential mobility particle sizer; FMPS Fast mobility particle sizer; ELPI Electrical low pressure impactor; NSAM Nano surface aerosol monitor; OPS/C Optical particle sizer/counter; CPC Condensation particle counter; TEM/SEM Tunnelling/Scanning electron microscope.

*Electron microscopy can only be applied if particle collection was conducted in a manner to allow calculation of the size distribution in the airborne state. The other measurement principles can be applied in situ in air.

Table 5
Brief overview on comparison results for nanoparticle monitors.

Instruments	Relative comparability	Setting	Source
SMPS vs. NSAM (Lung deposited surface area)	± 20%	Laboratory, different materials	Leskinen et al., 2012
SMPS, FMPS, CPC, ELPI (number concentration)	± 40%	Laboratory, different materials	Leskinen et al., 2012
SMPS, FMPS, ELPI (diameter)	± 30%	Laboratory, different materials	Leskinen et al., 2012
CPC (number concentration)	± 5%	Laboratory, NaCl, DEHS, soot particle	Asbach et al., 2012
CPC, various other (number concentrations)	± 30%, but can be also 600% for specific cases	Laboratory, NaCl, DEHS, soot particle	Asbach et al., 2012
SMPS, FMPS (diameter)	± 25%	Laboratory, NaCl, DEHS, soot particle	Asbach et al., 2012
SMPS, various monitor (LDSA)	± 30% only if particle size < 300 nm	Laboratory, NaCl, DEHS, soot particle	Asbach et al., 2012
SMPS, FMPS (diameter)	± 25%	Laboratory, NaCl, DEHS, soot particle	Kaminski et al., 2013
SMPS, FMPS (number concentration)	± 35%	Laboratory, NaCl, DEHS, soot particle	Kaminski et al., 2013
EEPS, FMPS, SMPS	± 40% up to 80% at high concentrations	Laboratory and field, soot particle	Zimmerman et al. 2014

SMPS-scanning mobility particle sizer, FMPS-fast mobility particle sizer, EEPS-engine exhaust particle sizer, CPC-condensation particle counter, ELPI-electrical low pressure impactor.

Table 6
Possible transformation processes for selected consumer product categories and MN applied in these products (Mitrano et al., 2015).

Product category	MN	Transformation processes
Textiles	Ag, ZnO, SiO_2, TiO_2, ENP coating	oxidation, dissolution, precipitation, UV-irradiation, incineration, release of MN
Sunscreens, cosmetics, personal care products, cleaning agents	Ag, ZnO, SiO_2, TiO_2, ENP coating	oxidation, dissolution, agglomeration, UV-irradiation, micellation
Paints and coatings	Ag, Ag zeolite, CNT, ZnO, SiO_2, TiO_2, CeO_2	oxidation, dissolution, agglomeration, UV-irradiation, release
Plastics and polymers	Ag, CNT, TiO2, ENP coating	UV-irradiation, incineration, dissolution, structural transformation, aggregation
MN in food sector: additives, supplements, containers and packaging	Ag, ZnO, SiO_2, TiO_2, CeO_2, ENP coating	Food: Dissolution, phase transformation, degradation, physical transformation Food packaging: dissolution, UV-irradiation, migration of MN from material
The energy sector, fuels and catalysts	Ag, CNT, ZnO, TiO_2, CeO_2	acid wash, incineration
Consumer electronics and semiconductors		
Air filter		UV irradiation, incineration, combustion

easy to handle and deliver reliable data. They normally determine LDSA and NC concentrations. A major drawback is that these devices can only be applied for particles in the size range from ca. 20–400 nm. The accuracy of instruments based on diffusive particle charging and electrical detection is lower for particle number concentrations than those counting particles e.g. CPCs. The reproducibility of CPC measuring particles in the range from 1 to 1000 nm is generally better than those of other devices if detection is done in the single particle mode.

The first devices for portable particle size distribution monitoring down to a few nanometer have been developed (Nanodevice, 2013) but their availability is still limited and further improvement needed. Standard SMPS or, for fast changing particle number concentrations and size distributions, an FMPS, are currently the best suited stationary measurement devices for these metrics.

The major shortcoming with respect to measurement devices and their applicability is that systematic guidance covering a wide range of different nanomaterial types is still lacking. This includes an overview about which methods and strategies are best and most effectively to be used for what purpose (material and setting specific).

3.2. Which particle metric?

The question of particle metrics to be used for exposure measurements is still a point of discussion. The point of best metric was never further debated in regulatory related guidance (e. g. NIOSH, 2011, Announcement 527). Possible particle metrics are number, surface area, volume and mass concentrations. Several reasons can be given as to why mass concentration is currently in the focus of regulation. Mass concentration is “conservative”; that is, it does not change from release, emission to exposure if deposition, dissolution, and other removal processes are neglected. This is not the case for the other metrics: LDSA and NC may change during transport, masking the direct link from

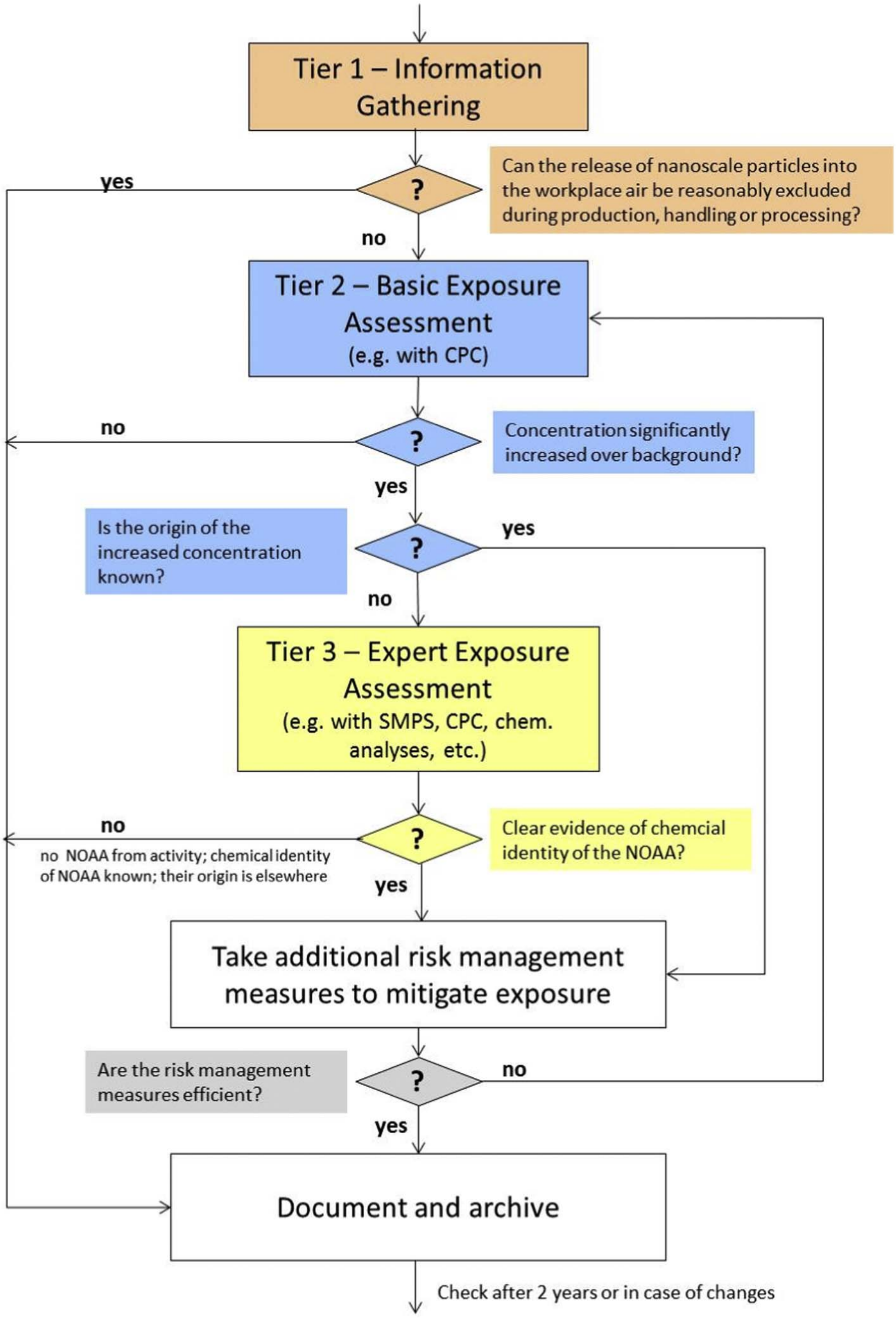

Fig. 3. Tiered approach according to OECD (2015)

source to exposure. Secondly, all chemical regulations are currently based on mass concentrations and extending this concept with the same metric is "easier" to implement than to introduce a new metric. However, the main reasons for using other metrics in exposure assessments are 1) possibly higher correlations with specific toxicity (in vitro and in vivo) and health endpoints, 2) higher detection sensitivity (e.g. number concentration) compared to the low mass concentration of nanomaterials, and 3) easiness of measurement and availability of devices for online personal exposure measurements (number and surface area measurements). Especially the first and the last are of high importance in the regulatory context. If a dose metric correlates better with the endpoint of interest than the „traditional "mass-based one, this should be considered in the regulatory framework as is the case for asbestos. Secondly, easy to handle, affordable and reliable measurement devices are essential for the implementation and hence for safety in the workplace.

Several studies on different particle metrics and health effects have been conducted. Results obtained from experimental studies as well as from epidemiological assessments did not show a more robust, significant correlation for PNC or LDSA than for mass concentrations (Schwarze et al., 2006; Stoeger et al., 2006; Soppa et al., 2014; Noël et al., 2016; Soppa et al., 2017). Hence mass concentration is still used most frequently in exposure and risk assessments.

The mode of action of fibres is based on the fibre paradigm and relates to fibre length, their biopersistence and rigidity (Nagai et al., 2011) such that in theory each single fibre can cause a genotoxic effect possibly leading to cancer. The high potency and the specific mode of action of fibres demands for a fibre number concentration-based limit values. Fibres, which are entangled or twisted, are not considered as being rigid, but those with a straight stiff structure may have the potency to act like asbestos. Only very few, not readily available or feasible methods to assess fibre rigidity are known (Poncharal et al., 1999;

Löffler et al., 2011). Whilst standards for fibres with diameters larger than 200 nm have been established, specific methods for CNT and other nano-scaled fibres must still be developed. General measurement strategies have been developed by Rasmussen et al. (2015) or Heunisch and Bachmann (2016).

3.3. Natural versus manufactured nanomaterials (MN)

One of the major challenges in (occupational) exposure assessment in the regulatory framework is how to differentiate between natural, incidentally generated nanoscale particles and manufactured nanomaterials. Monitors determining solely mass, number or surface concentrations cannot differentiate particles types and hence possible sources. Therefore several new developments have been made with regard to quasi online particle size dependent composition measurements (R'mili et al., 2011). Combining particle size and chemical composition information some degree of differentiation is possible. One example for a measurement device is the aerosol mass spectrometer, which can also detect higher elements and metals, and hence is becoming of greater interest for nanomaterial exposure assessment (Nilsson et al., 2015). This device is currently not sufficiently developed to be of direct use for regulatory purposes but indicates one way in which some of the issues can be tackled in future. One method more often employed for this purpose is offline single particle analysis by electron microscopy for morphology and chemical composition (Kuhlbusch et al., 2011; Laborda et al., 2016). However, these methods are very labour intensive and expensive, and for this reason should only be applied when other methods fail or if there is a particular concern.

3.4. Standard operation procedures

Another important prerequisite for conducting reliable and robust exposure assessments is the availability of well-developed guidance documents and standard operation procedures (SOPs). SOPs may relate to the use of the measurement devices or strategies on how to employ and interpret the results of the devices. Evaluations of these standards and SOPs have to be conducted to finally allow the determination of the reliability and reproducibility of an assessment strategy. This has so far been done only in few cases like in the SIINN ERA-Net project NanoIndEx (Asbach et al., 2016), the BMBF project nanoGEM (Asbach et al., 2012b) by NIOSH for the Nanomaterial Exposure Assessment Technique (Eastlake et al., 2016) and NANoREG (2017).

3.5. Tiered approach for exposure assessment

When looking into the details of exposure measurements, strategies and assessments it quickly becomes apparent that a full assessment for each workplace handling nanomaterials will not be possible. As a result, several methods were developed, published and some of them also tested during the last ten years. Reviews and updates are given in OECD (2015), Eastlake et al. (2016) and Brouwer et al. (2016). It has to be noted that a tiered approach cannot strictly be followed for highly toxic substances. Tier 1 may indicate the highly toxic substance and then Tier 3 may directly follow with specific measurement needs. Anyhow, the specific applicable regulatory requirements have to be followed for highly toxic substances, e.g. for fibres with carcinogenic potential.

The general steps in the tiered approach for exposure assessment, taking the combined OECD tiered approach (2015, see Fig. 3) as an example, is divided into 3 major steps: a) information gathering, b) basic exposure assessment and c) expert exposure assessment. The three steps are briefly described here.

3.5.1. Tier 1 - information gathering

This tier is mainly based on “paper work” that is, information gathering to decide if nanomaterials are actually used. If yes, how are they handled and is there a likeliness of release and subsequent exposure. Tier 1 is one step where a framework of release (Kuhlbusch and Kaminski, 2014; see also Section 2) can be used. A combination of information from the framework of release with specific workplace scenarios can be used as a first tier to assess if a relevant exposure may occur.

3.5.2. Tier 2 - basic exposure assessment

If Tier 1 indicates a possibly relevant exposure, then measurements should be conducted at that workplace using direct reading handheld monitors to detect if elevated particle concentrations (number or lung deposited surface area concentrations) are present. These measurements can be made using different monitoring strategies, e.g. using spatial or temporal variations in concentrations to be able to assess nano-objects and their agglomerates above a given general background concentration. This technique can also be used in combination with longer term monitoring in the case of mainly sporadic exposures. General information on measurement strategies at workplaces are e.g. given in DIN EN 689 (2016) and DIN prEN 17058 (2016).

3.5.3. Tier 3 – expert exposure assessment

This tier, which is the most labour-intensive and expensive tier, is only necessary when the first two tiers indicate a significant exposure of concern, or if particles of very high concern (e.g. carbon nanotubes) are being handled. Tier 3 has to be set-up according to the specific needs of the workplace and the material handled. This differentiation is needed to be able to clearly identify and quantify the nanomaterial of concern next to any background values. Some methods like online aerosol mass spectrometer may be useful for metal oxides, whilst CNT or carbon black need different methods and measurement strategies (e.g. Rasmussen et al., 2015).

The approaches Tier 2 and 3 often use temporal and/or areal changes in particle concentrations to identify hot spot sources and source strengths. The main differences in the tiers are the data quality and the strict ability to differentiate background from manufactured nanomaterials. Guidance on data quality and data evaluation are e.g. given by Brouwer et al. (2016) and Asbach et al. (2016).

Overall, the tiered approach as e.g. suggested in the OECD Document (2015) can be viewed as a robust framework whilst the actual guidance and SOPs detailing how to act according to the tiered approach have still to be further elaborated.

3.6. Exposure assessment values

When using a tiered approach, assessment values are needed to define when a higher tier has to be pursued. These kinds of assessment values must still be defined or developed (see also Brouwer et al., 2016). Nevertheless, general exposure assessment values for all types of MN independent of their source have been suggested for cases where no specific toxicity is to be assumed, e.g. 0.5 mg/m^3 for granular biopersistent nanoparticle as suggested by Announcement 527 (2016). These kinds of values can be used in the tiered approach. The drawback here is that current values discussed by NIOSH, BAuA and other regulating bodies are based on mass concentration and are therefore not directly compatible to the easy to use and sensitive devices measuring NC or LDSA.

Furthermore, in cases, when a differentiation is needed, such as specific MNs exhibiting particular toxicity like CNTs or exceedance of the exposure values, approaches and measurement strategies have been introduced into standards and guidelines by ISO-TS 12901 (2012, 2014) and OECD (2015).

3.7. Control banding tools and exposure modelling

For the control of exposure to chemicals, control banding tools help in estimating workplace exposure. Even though control banding and modelling tools to estimate workplace exposure are improving, comparability between the different tools is not always given (Bekker et al., 2016; Liguori et al., 2016). Additionally, evaluation procedures and real test values are needed in order to evaluate the robustness of the tools (Liguori et al., 2016). In general, control banding tools are currently not seen to be robust enough to be used legally binding regulation. They are mentioned as a tool in the regulatory framework for e.g. the assessment of human health in REACH (ECHA, 2012).

Modelling transport and transformation of particles after their release into air has been investigated in a few studies (Schneider et al., 2011; Asbach et al., 2014). The reason for not employing these models at workplaces regularly or in regulatory settings is the lack of efficiency. The input information needed is so high and detailed that highly trained people are needed. Additionally, it is not seen by the authors that easy to use, mechanistically based models will become available soon.

One of the major drawbacks of the currently used work place as well as consumer exposure models is lack of their comprehensive evaluation by comparison e.g. to real measurement data or exemplary exposure scenarios. A first attempt in this direction was conducted within the e-team Project (Lamb et al., 2015) for several model tools such as - ECETOC TRA v2 and v3, STOFFENMANAGER® v4.5, MEASE v1.02.01, EMKG-EXPO-TOOL and RISKOFDERM Version 2.1. Here the authors conclude “Comparison with measurement data suggested that the tools were generally conservative, but perhaps not always sufficiently so when compared with the reasonable worst case estimates as defined by the 90th percentiles of the exposure distribution”. Further information can be found in the final e-team project report (Lamb et al., 2015; Tischer et al., 2017; Van Tongeren et al., 2017; Fransman, 2017). Overall, the robustness and accuracy of the model still have to be assessed thoroughly to improve their use in the regulatory context.

3.8. *Exposure reduction measures*

A recent study by Schubauer-Berigan et al. (2015) showed that in industrial settings, the implementation of engineering controls and personal protective equipment (PPE) was often reversed. According to current legal requirements, PPE should only be used after all affordable engineering and organisational control measures have been set up. An exception is where these measures cannot be taken for organisational or technical reasons. The study showed a) a high usage of protective measures at all industries surveyed, and also at the investigated sites but b) the same frequency of occurrence of PPE-use compared to engineering control measures.

Effective technical measures often applied when handling nanomaterials and nano-powders, are increased ventilation in combination with the use of hoods (Lo et al., 2015). These technical measures often work very well, since airborne nano-scaled particles behave similar to gases. Investigations of hoods (Lo et al., 2015) also showed a high degree of protection against airborne exposure. Interestingly, as with larger particles, handling with powders with opened hoods allows a small portion of the particles to escape from the hood leading to immediate exposure. This has to be considered especially when handling materials with high toxicological potency. In the latter case glove boxes may be used.

When using PPE, the obvious question is if they are really protective, and how well and how easy they are in use. Generally, a loose fitting facial mask will not give sufficient protection against airborne nanomaterials (Rengasamy and Eimer, 2012). This example shows that not only the equipment performance itself is important, but also how it is actually used. Particle filtration is highly efficient for large particles due to impaction and for nano-scaled particles due to diffusional deposition. Lowest filtration efficiencies are mostly to be expected for the size range from 100 to 400 nm. Other important PPEs are clothes and gloves (NanoSafe, 2008; Kim et al., 2007; Rengasamy et al., 2008)

Glove tests sometimes show bad reproducibility (Vinches et al., 2016) which can even change from one lot to the other. One of the reasons for this can be micro fissures. Penetration through gloves is more likely for handling liquids. Penetration efficiencies in these cases were always lower than 5% and mostly lower than the detection limit. Certainly, appropriate gloves with regard to the handling of nanomaterials should be used and double-glove use will further reduce exposure. The same is valid for clothes. Penetration efficiencies can vary significantly depending on the type of clothes and the type of nanomaterial being used.

The performance, e.g. expressed as a penetration factor, of protective devices like filters, gloves and clothes can be investigated and properly assessed for normal use. Depending on filter types, penetration factors lower than 0.01% for breathing filter can generally be achieved. Loose-fitting powered air purifying respirators show a protection efficiency of even 10^{-6} (Koivisto et al., 2015).

4. Consumer exposure

4.1. *Nanomaterials in consumer products: data availability and quality*

In general only very few reliable data exist on the use of nanomaterials in different consumer products. Therefore, inventories like Woodrow Wilson are often used to get an overview on which nanomaterial containing products (http://www.nanotechproject.org/cpi/). However, this source of information is not complete, up to date, representative or verified. Furthermore materials are ranked according to the number of available products and not their tonnage on the market. According to the Woodrow Wilson Database nanosilver is among the most commercial relevant MN, however according to total estimated worldwide production of approximately 50 t per year it seems to be less significant (Piccinno et al., 2012). Recently in Denmark, the Nanodatabase (www.nanodb.dk) has been developed, in which the availability of nano-products in Europe has been updated. However, the data are based on voluntary reporting of the manufacturers of the products (Hansen et al., 2016). Only very few countries have obligatory product inventories, such as France, Belgium, Denmark and Sweden. In the EU, labelling of nanomaterials as constituents of nano-products is required for only a few types of products, such as food, biocides and cosmetics. It is therefore very difficult to get reliable information on which types of nanomaterials are really used in specific consumer products and in which amounts. In addition, there is hardly any reliable data on total tonnages of nanomaterials produced worldwide. All published studies so far use estimations. The EU Commission recently launched the EU-Nano-Observatory (EUON, https://euon.echa.europa.eu/), a website hosted by ECHA in which all information on nanomaterials in consumer products will be combined, i.e. information derived from legal registration/classification according to REACH, CLP and the Biocidal Product Regulation, as well as toxicological information derived from EU projects. As this website is currently set up, it is not yet clear to what extent it will serve as a EU wide nano-product registration and will satisfy the need for more accurate and detailed information in Europe.

4.2. *Consumer exposure assessment in REACH*

Within REACH an assessment of consumer exposure is only required, if there is any intended consumer use scenario. Requirements are that the production volumes of the substance exceed 10 tons/a and that it has a hazard classification. For this purpose, ECHA has released a guidance document (ECHA, 2016a) on specific methods for the calculation of inhalation, oral and dermal exposures for consumers, applicable also when only little information is available.

Fig. 4 shows a general workflow for consumer exposure assessment within REACH mainly describing consumer exposure for chemicals with little specific guidance for nanomaterials.

For a proper exposure assessment, a consumer exposure scenario with sufficient information on the user of the product as well as the product itself (type of product, characterization of the product is essential. A crucial aspect is the question whether there are nanomaterials

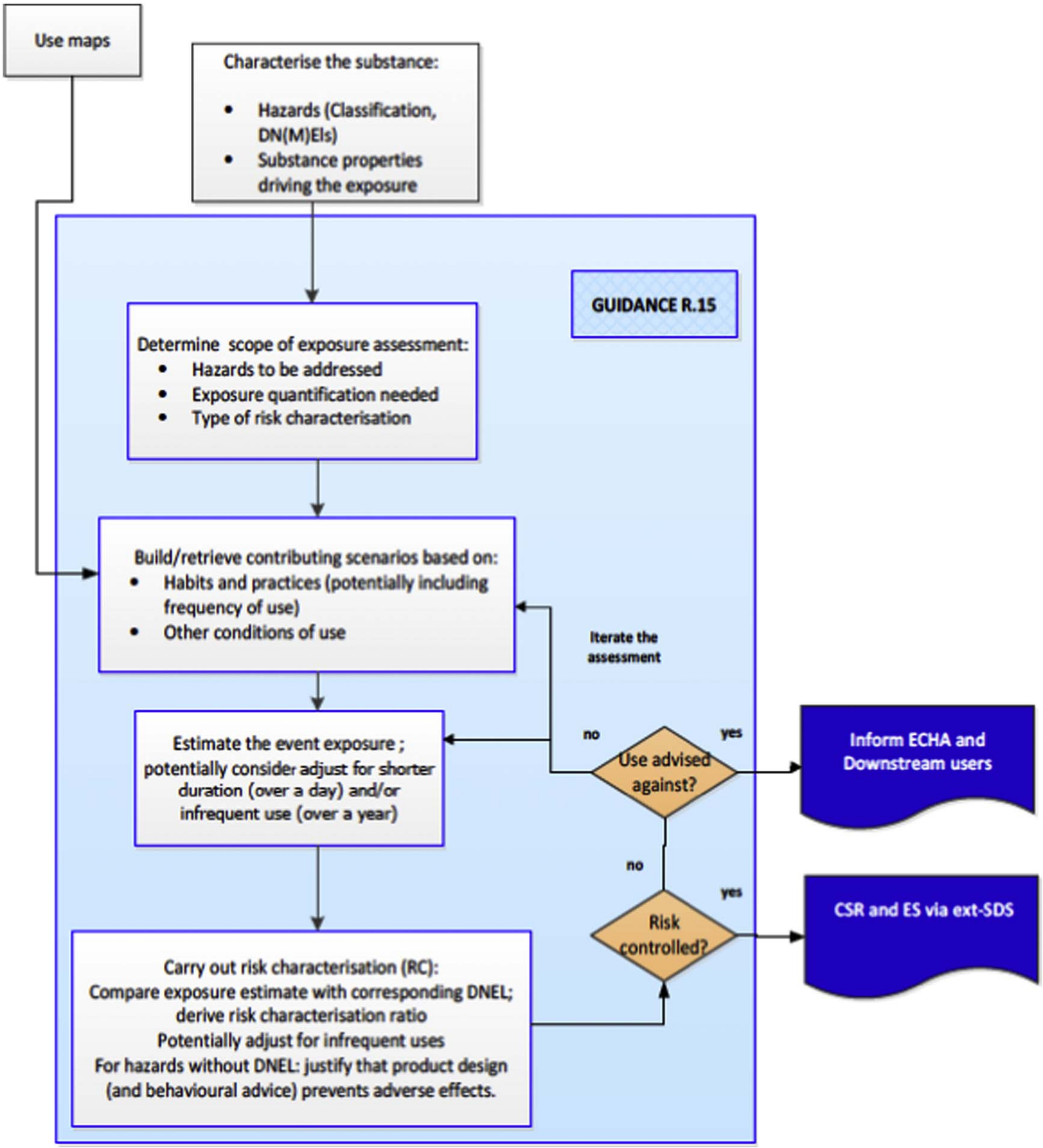

Fig. 4. A general workflow for consumer exposure assessment (from ECHA, 2016a, Chapter R.15)

present in the product and if so, which MN, in what concentration and what form. Also information on possible release of MN from the product is essential. A first release library was recently created by Koivisto et al., 2017 in which quantitative material releases from products and articles containing MN are described (Koivisto et al., 2017).

Exposure to consumer products normally cannot be monitored or enforced beyond the point of sale. This renders consumer exposure assessment more difficult than worker exposure because it often relies on modelling and assumptions, frequently conservative, rather than on measured data. The model parameterisation and assumptions are currently not harmonised and expert assessments are needed. Consumer exposure assessments cover the intended uses of a product but also needs to consider all reasonably foreseeable uses or misuses. In addition, aggregated exposure of the same MN across multiple products should be considered.

Another difference to worker exposure is the exposure route of concern. For consumer exposure, apart from inhalation, also other exposure routes are highly relevant. Therefore, a brief summary of studies on these routes is included here.

4.3. *Consumer exposure routes*

4.3.1. *Dermal exposure and uptake*

Dermal exposure may either occur from direct hand or body contact with a consumer product or article (e.g. jewellery, textiles, straps, belts, shoes) or from deposition of particles or aerosols from an airborne substance, from skin contact with residues of the substance after product use (e.g. residues on clothing after laundering or dry cleaning). A major product category for dermal exposure is cosmetics, which is regulated by the Cosmetics Regulation (EC) No 1223/2009. Dermal exposure (of all chemicals) is expressed in terms of the amount of substance per unit surface area of the skin exposed (mg/cm^2) or as dose (mg/kg body weight/day) on skin. As REACH only considers external exposure, derived no effect levels (DNEL) derived under REACH already need to take skin absorption into account.

The European Scientific Committee on Consumer Safety (SCCS) published specific guidance on how to perform risk assessment of nanomaterials in cosmetics with dermal absorption assessment as one key factor (SCCS, 2012). Although it is currently not clear which metric is currently the best dose descriptor for nanomaterials, mass based exposure is generally used for practical reasons but tests on skin absorption of nanomaterials should also be evaluated using different dose metrics according to SCSS. If no data on skin absorption is available, one needs to assume 100% absorption as a default.

In order to assess skin penetration of nanoparticles, different in vitro and in vivo methods can be applied. Several studies assessing nanoparticle skin absorption used the in vitro method as described in OECD TG 428 (2004).

Dermal penetration of TiO_2 nanoparticles has been assessed (in vitro and in vivo) in the SCCS opinion on nano-TiO_2 (SCCS, 2013). All these studies with different formulations show that TiO_2 does not penetrate into viable parts of the skin in relevant amounts. Typically, TiO_2 NPs can be detected only in the outermost *stratum corneum* layers and not in any viable parts of the skin, neither epidermis nor dermis. In addition, UV sunburnt, compromised skin was also studied. Details, as well as all considered primary studies are described in the SCCS opinion on nano-TiO_2 (SCCS, 2013). It should be noted that inhalative exposure has been specifically excluded from the SCCS assessment.

In contrast, another study for nano-scaled SiO_2 using non-guideline methods shows some forms of nano-SiO2 can penetrate the outermost skin layers and reach viable parts of the epidermis, and even the dermis. Nano-SiO_2 was also detected in dendritic cells. In addition, there is some evidence that formulation has an effect on uptake of SiO_2, which was not the case for TiO_2 NPs. Details, as well as all considered primary studies can be found in the SCCS opinion on nano-SiO_2 (SCCS, 2015).

Only few studies investigated the release of nano-silver and nano-TiO_2 from the textiles into artificial sweat (von Goetz et al., 2013), which simulates the release during consumer use. This study found that release of TiO_2 was only minor whilst the authors could detect significant amounts of released silver. For silver the authors calculate maximal amounts of 17.1 (total silver) and 8.2 (Ag $<$ 450 nm) μg/kg body weight. For TiO_2, the exposure levels amount to maximal 11.6 μg/kg body weight for total (mainly particulate) TiO_2.

A good overview on dermal absorption of nanomaterials is given in a Danish EPA report (Poland et al., 2013). Their conclusion on dermal absorption of nanomaterials is that whilst there are many conflicting results, on balance the literature seems to suggest that absorption of particles in the nano-range through the skin is possible, but it occurs to a very low degree.

4.3.2. *Oral exposure and uptake*

Oral exposure of MN in consumer products may include uptake of residues from cosmetics or dishwashing products or may occur as a consequence from migration of a chemical from an article (e.g. chewing or licking of toys for children). Another route of oral exposure is clearance of the lung transporting materials out of the lung with the mucus which is ultimately swallowed. Oral exposure of MN via food or food contact materials (FCM) is the most relevant source but is only addressed briefly here. Information can be found in the scientific opinion of EFSA on risk assessment of chemicals in FCM (EFSA, 2016; EFSA, 2011). EFSA has published scientific opinions on a few nanoforms for the use in food and FCM such as titanium nitride (EFSA Journal, 2012), SiO_2 (EFSA Journal, 2014) or ZnO (EFSA Journal, 2016). Typically, in these cases no release of nanomaterials from the food contact matrix to the food could be demonstrated.

A few projects have addressed nanomaterial consumer exposure from food (EU project NanoLyse, http://www.nanolyse.eu/default.aspx) and some also studied release from food contact materials. Often the release of nano-silver is studied (e.g. Mackevica et al., 2016), which frequently show that silver ions can be released from products. The study of Mackevica et al. uses an experimental setup according to EU regulation 10/2011. Some migration of nano-silver from the plastic to the food could be demonstrated in this study, it should be noted that nano-silver has not been assessed by EFSA. Therefore, the use of nano-silver in plastic food contact material is not eligible within the EU. Some other nanomaterials (e.g. ZnO, nano-clay) are also investigated but to a smaller extent in published literature.

Furthermore, for assessing oral exposure to nanomaterials one has to consider changes of the nanomaterial occurring during the gastrointestinal tract passage. In consequence, a few nanomaterials have been shown to dissolve completely in the stomach and to reform in the duodenum. This can be assessed in vitro by using an artificial digestion fluid model (Peters et al., 2012; Walczak et al., 2012; Böhmert et al., 2014). The analysis can also be performed in the presence of relevant food simulants (Lichtenstein et al., 2015).

It should be noted that the Danish EPA has carried out a project to assess consumer exposure to nanomaterials, which contains information on different types of nanomaterials in different product types, and considering different routes of exposure(Larsen et al., 2015).

4.3.3. *Inhalative exposure*

Currently also for consumer exposure to nanomaterials the inhalative route is regarded as that of main concern. Examples of relevant consumer products for this exposure route are spray products, where one furthermore needs to discriminate between propellant sprays versus pump sprays, powders (e.g. make-up) and exposure after emission from articles or paints.

Exposure by inhalation is normally presented as an average concentration over a reference period of time, which will normally be the duration of one single use event. Thereafter the frequency of such use-events needs to be considered. However, peak exposure during short peaks requires more particular consideration. A few projects have specifically addressed this exposure. Examples are the Swiss NanoSpray projects run by ETH and EMPA (NanoSpray I, 2008–2010, NanoSpray II, started 2011). In addition, consumer exposure from spray products containing nanomaterials was also addressed in the German funded project nanoGEM (Riebeling et al., 2016).

4.3.4. *Other exposure routes*

In special cases also other routes of exposure have to be addressed. This may refer to exposure via eyes (this may be relevant for mascara, which can contain nano-carbon black) or intradermal routes for tattoos, where some of the pigments may contain nano-scaled particles. However, there is no specific knowledge about these exposure routes for nanomaterials available.

4.4. *Tiered approach for consumer exposure*

Parallel to the suggested tiered approach to assess workplace exposures a similar approach could be pursued for exposures to consumer products. The tiers could be:

Tier 1: Information gathering if the product contain nanomaterials;

Tier 2: Information from above release test methods;

Tier 3: Simulated use of products under well-defined laboratory conditions.

Anyhow, such type of tiered approaches for assessing consumer exposure to nanomaterials in consumer products still has to be explored.

4.4.1. *Modelling consumer exposure*

Only a few models are available for estimating consumer exposure to nanomaterials. ECETOC TRA (developed by ECETOC) covers all relevant exposures (environment, consumer and worker) but was not specifically developed for nanomaterials. This model as well as some other models may be used in the framework of REACH to register nanomaterials. In the following some exemplary information are given about two Dutch models which are frequently used for consumer exposure assessment:

ConsExpo (www.consexpoweb.nl) is a computer programme developed by the National Institute for Public Health and the Environment (RIVM) that enables the estimation and assessment of exposure to substances from consumer products such as paint, cleaning agents and cosmetics. ConsExpo is used within and outside Europe by governments, institutes and industries to assess the exposure to chemical substances from consumer products. ConsExpo is applied in the EU for the assessment of industrial chemicals (REACH) and biocides.

The programme provides insight into exposure via inhalation, via the skin, or by oral intake. Users choose the most appropriate scenario and fill in exposure parameters such as body weight and exposure duration. The programme consists of both screening models and higher tier models for an estimation of exposure.

Information about circumstances under which consumers are exposed to chemical substances from consumer products is available in so-called fact sheets. For several product categories so-called default parameter values are provided which can be used as a basis for the calculations in ConsExpo. These default values are also available in the database that is coupled to ConsExpo. By means of the fact sheets, the exposure assessment may be carried out in a transparent and standardized way.

Although this software has been developed for conventional chemicals, the ConsExpo model can be used for exposure estimation of nanomaterials via the oral and dermal route. For inhalation exposure to nanomaterials, a new module of ConsExpo has been developed by RIVM in 2015: ConsExpo nano (www.consexponano.nl).

ConsExpo nano was developed as a new tool to assess consumer exposure to nanoparticles from consumer sprays and powders and is based on the ConsExpo model for conventional substances in spray products. During the use of a consumer spray product, the nanomaterial that is released from the spray may become airborne as part of the spray aerosol or as individual particles. To estimate the alveolar load arising from the use of nano-enabled spray products or powders, ConsExpo nano combines models that estimate the external aerosol concentration in indoor air, with models that estimate the deposition in, and clearance of, inhaled aerosol from the alveolar region. Furthermore, ConsExpo nano expresses exposure estimates in a variety of dose metrics, allowing the exposure assessor to evaluate various alternatives.

5. Environmental exposure

Release of nano-objects may also lead to environmental exposure. In particular weathering and leaching from nanomaterial waste and nanomaterials used for objects in the environment like catalytic paints are relevant processes which may lead to environmental exposure. Tools and test method being capable of predicting release and transformation of MN are important since not all MN (and all characteristics) can be tested experimentally. First developments in this direction were done within EU projects like MARINA, SUN and NanoHouse. Review publications from these projects give a very good overview on the current state of knowledge on environmental release and exposure (e.g. Cornelis et al., 2014; Baalousha et al., 2016; Peijnenburg et al., 2015; John et al., 2017).

It has to be noted that the above projects and developments therein relate to release and modelling but not to direct measurement of engineered nano-objects in the environment. A recent review on models being developed and used in the regulatory context is from Nowack (2017). The reason for focussing on models for environmental exposure are the problems in clearly identifying specific MNs in environmental matrices which in some cases are practically impossible. One of the few studies showing a release into the environment were measurements were done in the river Danube downstream of a swimming area (Gondikas et al., 2014). By comparing measurements during season and off-season they clearly demonstrated the increase in TiO_2 particle concentration in the river. Electron microscopic analysis of the particles confirmed that the source of the elevated concentration was related toTiO_2 in sun blockers.

One method quite often discussed for the use of MN measurements in environmental fluids is the use of field flow fraction (von der Kammer et al., 2011). This method is based on the separation of particles by their size and subsequent determination and possibly chemical analysis. It is versatile and sensitive, in particular when coupled to ICP-MS detectors, which is, however, possible only for some MN types. Other major drawbacks for a wider use are the high costs, need of very well trained people and difficulty in separating natural from engineered nano-objects. Hence and due to the very low ambient concentration the use has so far been limited. Overall, methods to detect and quantify MN in the environment are still in the development and evaluation phase.

In consequence, very little to no information concerning the exposure of the population via the environment are available. The only way to derive ambient MN concentration is via modelling (Nowack, 2017) or sampling close to sources like in the above mentioned example at the river Danube (Gondikas, 2014)

Other sources of environmental exposure (e.g. effluents from sewage treatment plants, abrasion from tires, disposal and incineration of waste, direct application of MN in agriculture etc.) will be discussed in a companion paper by Nowack (2017).

6. Summary

Overall, considerable progress has been made in various areas of exposure assessment especially during the past ten years. Measurement devices and strategies are becoming more readily available and measured values more robust with comparabilities in the range of e.g. 30–50% for airborne particle measurements. The measurement devices also became easier in handling and more affordable with prices below 10 k€ mainly for particle number and surface area measurements. These developments are a prerequisite to enable the implementation of exposure measurements for nanomaterials into regulation. Anyhow, particle speciation characterize single particle composition and to facilitate or even enable the identification sources is still an area where developments are needed.

Exposure metric: Tiered approaches and assessment values for workplace exposure are today further advanced, but still lack major agreements to be able to improve assessments and, where needed, regulation. Mass concentrations are currently mainly used in workplace and regulatory risk assessments, even though a significant amount of workplace measurements have been conducted determining particle number or surface area concentration. In some cases the latter metrics may also be more relevant for selected health end points. Measurement methods and strategies for nanofibres will have to be based on number concentration like asbestos, but are significantly less developed than those of nanoscale particles.

Reliable data, measurement methods and strategies for the estimation of consumer and environmental exposure are still in the infancy. Consumer exposure is and cannot be measured on a regular basis. The major problem for environmental exposure measurement is the lacking possibility on determining MN in environmental matrices on a routinely basis. Both points show the difficulties and explain the higher exposure uncertainties for consumer and public exposure via the environmental. For consumers one way forward could be improved guidance for assessing consumer exposure to nanomaterials within e.g. REACH, Cosmetics Regulation and Food legislation. State-of-the-art assessing environmental exposures are models considering also transport and transformation of MN. These models need further evaluation.

Prerequisite for exposure is the release of MN into the exposure media. Hence, test methods facilitating the assessment of likeliness and forms of release have been advanced to standardization in recent years. A framework defining which methods are needed, what should be their output and how the data can be adapted for use in e.g. modelling and safer by design has to be further developed to advance prospective exposure assessment. For exposure and risk assessment purposes, release rates and type of fragments should be identified and tested (in addition to the pristine material) and methods to link theses release data to realistic exposure concentrations further developed.

Along with these developments, real life studies are still needed to allow the evaluation of the models and tiered assessment strategies presented in this review.

Overall, many developments for use in the regulatory framework have being made and some of them are already taken up in harmonisation and standardization bodies, in guidance to regulation as well as in a few cases in legally binding regulation. This development of bridging scientific developments with regulation has to be further pursued and interaction between those intensified to facilitate adaptions in regulation where needed and appropriate.

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