Chapter 2 Assessment of Human Exposure to ENMs

Araceli Sánchez Jiménez and Martie van Tongeren

Abstract Human exposure assessment of engineered nanomaterials (ENMs) is hampered, among other factors, by the difficulty to differentiate ENM from other nanomaterials (incidental to processes or naturally occurring) and the lack of a single metric that can be used for health risk assessment. It is important that the exposure assessment is carried out throughout the entire life-cycle as releases can occur at the different stages of the product life-cycle, from the synthesis, manufacture of the nano-enable product (occupational exposure) to the professional and consumer use of nano-enabled product (consumer exposure) and at the end of life.

Occupational exposure surveys should follow a tiered approach, increasing in complexity in terms of instruments used and sampling strategy applied with higher tiers in order tailor the exposure assessment to the specific materials used and work-place exposure scenarios and to reduce uncertainty in assessment of exposure. Assessment of consumer exposure and of releases from end-of-life processes currently relies on release testing of nano-enabled products in laboratory settings.

Keywords Engineered nanomaterials • Occupational exposure • Consumer exposure • Tiered approach

2.1 Occupational Inhalation Exposure Assessment of Engineered Nanomaterials

2.1.1 Why Carry Out an Exposure Assessment?

Exposure assessments can be carried out for a variety of reasons. For example, for (i) regulatory risk assessment, i.e. to provide evidence that exposures are below Derived No Effect Levels (DNELs) under the EU REACH (Registration, Evaluation, Authorization and Restriction of Chemicals) regulations; (ii) for risk management,

A.S. Jiménez • M. van Tongeren (⊠)

Centre for Human Exposure Science (CHES), Institute of Occupational Medicine, Research Avenue North, Riccarton, Edinburgh EH14 4AP, UK e-mail: Martie.VanTongeren@iom-world.org

[©] Springer International Publishing AG 2017

L. Tran et al. (eds.), *Modelling the Toxicity of Nanoparticles*, Advances in Experimental Medicine and Biology, Vol. 947, DOI 10.1007/978-3-319-47754-1_2

i.e. by checking whether exposure is below Occupational Exposure Limits (OELs); (iii) to check the effectiveness of exposure control measures; (iv) to contribute to epidemiological studies or health surveillance.

Strategies for conventional chemicals are reasonably well established and in general, relatively easy to measure mass-based metrics are used for exposure assessment. In contrast, for engineered nanomaterials (ENMs) there are no established standard measurement protocols and no consensus on the most appropriate single exposure metric. In fact, the REACH Implementation Projects on Nanomaterials (RIP-oNs) recommended using more than a single metric [1]. The design of the measurement strategy will depend on the purpose of the study. ENMs are manufactured in many variations of size, shape, structure, and surface modifications. Exposure to ENM can occur as primary particles, aggregates or agglomerates (usually referred as nanostructured particles), as well as ENMs embedded in a matrix. The exact physical-chemical composition of the ENM can change across its lifecycle and can also change over time following release into environmental media to such an extent that exposure measurement is a challenging process.

There is strong evidence of a particle size-related and morphology-related health risk following inhalation of some aerosols. Fibre-shaped nanomaterials such as carbon nanotubes (CNT) and other high aspect ratio nanomaterials (HARN) such as graphene, nanoclay or silver nanowires, have been shown to pose particularly high risk to the respiratory system after inhalation exposure [17, 23, 47, 50, 54, 56]. Relevant information about exposure to nanomaterials can be gained from number and surface area concentration measurements. In addition, further characterisation of chemical and physical properties of airborne particles collected on filter samples is recommended [40].

2.1.2 Occupational Exposure Limits for Nanomaterials

There are very few OELs specifically for ENMs. For carbon nanotubes (CNT) (all types) and carbon nanofibers (CNF), NIOSH advocates a Recommended Exposure Limit (REL) of 1 μ g m⁻³ elemental carbon in the respirable fraction as an 8-h time-weighted average (TWA). This REL was established based on a review of animal studies and other toxicological data relevant to assessing the potential non-malignant adverse respiratory effects of CNT and CNF [41]. NIOSH recognizes that the REL level may not fully protect workers' health but will help to minimize the risk of developing lung disease. In order to test compliance with this mass-based limit, NIOSH recommends measurement of airborne elemental carbon as a proxy for CNT/CNF, according to the NIOSH method 5040 [37].

NIOSH also recommends a REL of 0.3 mg/m^3 for ultrafine (including nanoscale) TiO₂ as a TWA concentration for up to 10 h/day during a 40-h work week [40]. When the particulate exposure consists predominantly of TiO₂, then the NIOSH method 0600 [38] for measuring fine and ultrafine TiO₂ is recommended. If there is also exposure to other airborne particulates or when the size distribution of TiO₂

(fine vs. ultrafine) is unknown, other measurements and/or analytical techniques may be needed to characterize ultrafine TiO_2 . Either NIOSH Method 7300 based on ICP-AES [39] can be used to analyse TiO_2 , or electron microscopy, equipped with X-ray energy dispersive spectroscopy (EDS), to identify TiO_2 particles.

It is argued that for particles smaller than 100 nm due to their low mass compared to their larger particle number and surface area, mass may not be the most appropriate metric for health risk assessment [16, 44] and surface area is the preferred probably most relevant exposure metric [25]. NIOSH (like ISO) also acknowledges that surface area may be a more appropriate metric than mass; however, since there are currently no established analytical methods to assess specific particle surface area for TiO₂, mass-based measurements are accepted as a surrogate metric.

The British Standard Institute (BSI) has proposed bench-mark values for four types of ENMs [12]. For fibrous materials, the bench-mark value (0.01 fibres/ml) is based on the clearance limit in the UK for asbestos removal operations. For other ENMs, the bench-mark values are derived from the OEL of the corresponding micro-sized bulk material. For insoluble ENM this is $0.066 \times OEL$, for soluble is $0.5 \times OEL$ and for carcinogenic, mutagenic, asthmagenic or reproductive toxin in bulk form ENM this is $0.1 \times OEL$. It should be noted these bench-mark values are for guidance only and should not be considered to representative of safe workplace exposure levels, as they have not been linked to toxicological end-points. They have been developed under the assumption that the hazard potential of the nanoparticle form is greater than the micron-sized particle. Van Broekhuizen et al. [52] introduced the concept of bench-mark values and proposed so called non-substance specific nano reference values. When the exposure exceeds an 'action level' more specific measurements or exposure controls are required.

In Germany, the Institute for Occupational Safety and Health of the German Social Accident Insurance (IFA) has established limit values for airborne particles between 1 and 100 nm based on the particle number concentration. For metals, metal oxides and other biopersistent granular ENMs with a density over 6,000 kg/m³, concentrations should not exceed 20,000 particles/cm³. For ENMs with densities below 6,000 kg/m³ the concentration (1–100 nm) should not exceed 40,000 particles/cm³ [24].

2.1.3 Measurement Devices

There are a number of different techniques to measure real-time particle number, mass, size distribution and surface area of airborne particles covering the particle size range from 3 nm to 20 μ m. However, the principle of operation of particle size instruments limits the particle range that a single instrument can measure, and therefore in order to acquire the full size distribution a range of different instruments is employed. It should be noted that despite the fact that the definition of ENM refers to materials with one dimension <100 nm, their agglomerates and aggregates can reach micron sizes and therefore measurements should – cover both nano- and

micron-size ranges [45]. There is currently no agreement on the upper size limit that should be assessed. It is likely that agglomerates/aggregates of nanosized particles will be largely in the respirable fraction ($D_{50} < 4 \mu m$). As well as being present as agglomerates/aggregates, ENMs can be scavenged by large background particles and ENM can also be released as part of relatively large particles consisting mainly of the matrix in which the ENM is embedded. High aspect ratio nanomaterials such and CNT and graphene may also be characterised by one dimension in the nano-size range but have large (>4 µm) physical sizes and lengths in the micron-size range [41, 47]. Hence, in addition to measurement of the respirable fraction, it may also be appropriate to include the inhalable fraction (D_{50} up to 100 µm).

Condensation particle counters (CPC) are the most common instruments used to measure the total (i.e. not size resolved) particle number concentration. They are available as portable and hand held devices making them suitable for screening assessment. The size range can be from up to 2.5 nm to 10 μ m depending on the model. CPCs can be used in combination with a differential mobility analyser (DMA) to measure size – resolved particle number concentrations.

CPCs generally have two counting modes: a single particle count mode (up to $10^4 - 10^6$ particles cm⁻³) where each particle is counted individually and the photometric mode for concentrations above 10⁶ particles cm⁻³ where the light scattered by all particles is measured and compared with calibration levels. Time resolutions are often down to 1 s measurement intervals. The accuracy of the single particle count mode is usually ± 10 , and the photometric mode is less accurate (± 20). Accuracy of the CPC may also depend on the condensation fluid and particle. For example, the accuracy in the photometric mode differs between hygroscopic and hydrophobic particles when water is used as the condensation fluid. In recent years portable electrical diffusion chargers (e.g. DISCmini, Partector, NanoTracer) have been developed which can be used for personal monitoring. The electrical current, stemming from unipolar diffusion charged particles, is coincidentally proportional to the lung deposited surface area (as long as the particle size range is within 20 nm $\leq d_p \leq 400$ nm) [4]. In addition these instruments also provide estimates of the total number concentration (usually 10-300 nm and or up to 10 µm in the case of the Partector), along with the mean particle diameter. Size-resolved instruments use electrical mobility analysers or differential mobility analysers. The most frequently used instruments are the FMPS (Fast Mobility Particle Sizer), and the SMPS (Scanning Mobility Particle Sizer). The Electrical Low Pressure Impactor (ELPI) can also be used to estimate the mass if the charge and the density of the particle are known and has the additional advantage that airborne particles are collected to allow for off-line analysis.

Most of these instruments are calibrated with spherical, compact, non-porous particles of a specific density. However, nano-sized particles and their agglomerated/aggregated forms tend to have a fractal-like structure and this can affect the accuracy of the measurements taken by these instruments. This type of instrumentation will also have limitations for the assessment of releases of fibre or plateletshaped nanomaterials. Instrument-specific effects such as counting efficiency (e.g. CPC) and multiple charging (e.g. SMPS, FMPS) can also affect the measurement accuracy.

2 Assessment of Human Exposure to ENMs

Since the instruments are calibrated with specific particles they only provide an equivalent diameter: electrical equivalent mobility diameter when sizing is by an electric field, diffusive (or thermodynamic) equivalent diameter, thermophoretic equivalent diameter or aerodynamic equivalent diameter for separation by impaction. For inhalation exposure the aerodynamic diameter is the most relevant equivalent diameter in the size range above approximately 100 nm. However, for particles below 100 nm diffusion due to Brownian motion is a more dominant deposition mechanism in the respiratory system and therefore the mobility-equivalent diameter is more relevant [27]. However, it is still unclear how the shape and density affect the electrical mobility diameter (and any other equivalent diameter) and therefore for nanofibres and nanoplates further studies are required to understand how they behave following inhalation [25].

Several studies have compared the performance of these devices [2, 22, 29, 53] using different aerosols morphologies and concentrations and found differences for the total number and the sizing of up to 30 %.

As stated above, the range of instruments deployed in nanoparticle detection should not be restricted to instrumentation covering the ENM primary size since airborne ENMs easily agglomerate into particles larger than several hundred nanometers. Aerodynamic Particle Sizers (size range 0.5-20 µm) using a time-of-flight light-scattering technique that measure aerodynamic diameter in real time can be usefully applied in exposure assessment. Aerodynamic diameter is a significant aerosol size parameter as it determines the particles' behaviour while airborne. Particle classification results from differences in the mobility of particles based on their size, density and charge as they travel through an optical detector. Results are presented as aerodynamic equivalent diameter, defined as the physical diameter of a unity density sphere that settles through the air with a velocity equal to that of the particle in question. Particles that have the same aerodynamic diameter will exhibit the same airborne behaviour and knowledge of the aerodynamic diameter subsequently allows determination of where the particle will be deposited in the human respiratory tract [13] and whether the particle will penetrate a filter, cyclone or other particle-removing device.

Measurements taken with direct reading instruments are useful to study variations in the metric assessed and size distribution during nano-related activities for comparison with background values. However, results of direct reading instruments alone should be interpreted with extreme caution [11, 15] in particular when used to derive mass related values for assessment of the exposure dose.

Another aspect that should be taken into consideration when using these instruments for exposure assessment is that they do not discriminate between the ENM and any other nano-sized particles present in the environment. Therefore to confirm the presence of the ENMs, characterization according to structure, size and morphology (Scanning/Transmission electron microscopy (SEM/TEM) and chemical identification (e.g. Energy Dispersive X-Ray (EDX); X-ray Photoelectron Spectroscopy (XPS), X-ray fluorescence (XRF)) of the particles collected on a filter is required. SEM or TEM are the most common methods used for particle characterization. However, SEM/TEM only provides information on the surface of a sample and therefore will not register ENM embedded in a matrix (e.g. polymer fragments with CNT). For nanocomposite materials atomic force microscopy (AFM) has been proved useful to characterize the ENM below the surface of composites [28, 59]. There are very few samplers specifically designed to collect the nano size fraction (<100 nm). Two samplers allow particle collection directly on the TEM grid: The Aspiration Electron Microscopy Sampler designed by VTT Technical Research Centre of Finland (from where it is commercially available) and the Mini Particle Sampler (MPS) developed by INERIS and distributed by EcoMesure.

2.1.4 Exposure Assessment Approaches of Engineered Nanomaterials

In contrast to conventional chemicals, where there are international standards for measuring, analysing and reporting of occupational exposure, for ENMs no established standard methods are available.

The International Standard Organization issued some guidelines in 2007 [25] and 2011 [26]. The reports provide very useful information on the available characterization methods but do not include details on how to analyse and interpret the measurement results and how to differentiate ENM from other nano-sized particles present in the workplace. In recent years several approaches have been published [3, 5, 6, 8, 35, 36, 40, 41, 57] and a number of initiatives have emerged across the nano-safety community to harmonize and standardize measurement strategies for ENMs. A series of international workshops "Global Harmonization of Measurement Strategies for Exposure to Manufactured Nano-Objects" have been organised since 2012 [9]. The European partnership of Occupational Health and Safety research (PEROSH) group has created a Nano Exposure and Contextual Information Database (NECID) to collect exposure measurement in a harmonized way.

These publications and workshop discussions formed the basis for the development of harmonized tiered approach published by the Organisation for Economic Co-operation and Development Working Party on Manufacture Nanomaterials (OECD WPMN SG8) [43]. The European Committee for Standardization is also preparing a document: 'Workplace Atmosphere-Assessment of inhalation exposure to manufactured nano-objects and their agglomerates (NOAA)' (CEN TC 137).

Most of the measurements strategies suggest a tiered approach:

- In the first tier contextual information on the materials, activities and exposure factors (e.g. amount of material used, ventilation, protective equipment, number of workers, frequency of exposure) is gathered to confirm that work with ENM is being carried out and exposure is possible.
- In the second tier, the concentration of airborne nanomaterials in the workplace is measured using a non-size selective real time portable particle number concentration instrument (e.g. CPC, NanoTracer, DISCmini, NanoCheck). The concentration during the activity is compared to background concentrations to assess

any potential increase in the particle number during the handling of the ENMs. In addition, some of the approaches recommend the collection of filter samples for off-line analysis using SEM or TEM coupled with a chemical identification technique. This helps to discriminate between the ENMs and nano-sized background particles. If activity concentrations are significantly increased over the background, the assessor may choose to evaluate the risk management measures and repeat a tier two assessment or to move directly to a tier three assessment.

• During a tier three assessment a more detailed survey is carried out which may include the measurement of personal exposure and/or the use of more complex equipment that provide real-time data on size-resolved particle number concentrations (e.g. FMPS, SMPS, ELPI), particle mass and/or surface area.

The main challenges highlighted in these approaches are (1) to distinguish the ENM from the background NMs (natural or incidental materials generated during the process, e.g. polymer particles release during extrusion); (2) to decide when to move from a basic survey to an in-depth campaign; and (3) to estimate quantitative exposure concentrations that can be used in health risk assessment.

Background particle concentration (especially when measured as particle number concentration) usually has a high spatial and temporal variability as they are affected by multiple emission sources (e.g. passing vehicles or nearby processes [34].

The approaches indicate three main strategies to assess the background:

- To measure during the activity under the same conditions but without using the ENM under investigation. This type of background allows determining the contribution of process-generated nano particles and therefore is the preferred method. However, this approach is not often feasible (e.g. for bagging activities).
- Far-field background: measurements collected at the same time as the activity in a place where no contribution of ENM is expected. This background concentration does not allow differentiation of process-generated nano particles and ENMs.
- Before & after the activity: again background measurements collected in this way do not allow differentiation of process-generated and other nano particles (e.g. from vehicles) and the ENMs of interest.

The nanoGEM approach [3] proposed to subtract the arithmetic mean (AM) of the background particle number concentration (measured for at least 45 min) from the AM measured during the activity. If the difference of the activity minus the background is larger than three times the SD of the background then release (if measurements are collected near the source) or exposure (if measurements are collected near the breathing zone of the operator) can be confirmed. The assumption is that that the background concentration will remain stable. However in practice this is may not be the case and this approach may not be applicable. However careful study design and interpretation can enable discrimination from the background in some circumstances. Considering the multiple sources of NMs in the workplace and the challenges to identify the ENM of concern, it is important to gather contextual information on other sources that could generate airborne nanoparticles.

Another important issue when carrying out a measurement survey is where to locate the measuring equipment in relation to the processes being monitored. Most studies target measurements areas in close proximity to the ENM source (<30 cm). While this is informative to determine whether there is emission of nanoaerosols into the workplace atmosphere, it is usually not representative of workers' exposure. Aerosol concentrations change over time due to deposition, diffusion and the effects of ventilation. This is particularly important for nano-sized aerosols due to their high diffusion rates and the effects of agglomeration and scavenging by background particles resulting in lower concentration and a shift of the size distribution. Consequently, measurements near the source or at any fixed point may not represent accurately the exposure of workers. Considering that only a few personal monitors are currently commercially available, the assessment of personal exposure is quite challenging. In this aspect modelling can be a very useful tool for exposure assessment and some advances have been made in relation to modelling of airborne nanoparticles in the work environment (both in field and theoretical; [19, 33, 48, 49]). In addition, if nanoaerosols are released into the workplace environment, they may deposit on work surfaces and act as a secondary exposure source to workers [55].

Regarding the decision criteria to move from a basic assessement to an in-depth monitoring survey the different approaches highlight different considerations. Witschger et al. [57] argues that the decision to carry out an in-depth monitoring campaign has to be taken considering the knowledge and experience of measurement of nanoaerosols, availability of instruments and methods, reachability of working location, compatibility of the instruments with the working environment and existence of previous measurements from the same place. Their basic level also includes chemical analysis of collected filter samples (e.g. TEM + EDX) in addition to CPC measurements. They also suggest that if the measurement campaign is likely to be challenging due to the working environment, release studies in a laboratory (e.g. dustiness measurement) can be carried out instead.

Brouwer et al. [8] proposed to divide the particle number concentration into those <100 nm and >100 nm. For both size fractions the decision to move to tier three should be based on a Student t-test on the concentrations during the activity and background; the ratio of those concentrations, the results from the TEM and EDX analyses and observations of the activities/processes taken place at the work place (Table 2.1).

Brouwer et al. [10] highlighted that data from direct reading instruments with short measurement intervals are autocorrelated and therefore the use of parametric methods, which are designed for independent data, is not appropriate. ARIMA (Autoregressive Integrated Moving Average) models could be used to estimate whether the activity has an effect on the level of particles compared with background levels [31, 32].

As part of the 7th Framework Project MARINA (Managing the Risk of Nanomaterials, http://www.marina-fp7.eu/) an exposure assessment strategy specifically developed for human risk assessment was developed. In this approach, also consisting of three tiers, the decision to move to a higher tier is not based solely on

	Ratio				
p-value	AM-nanoactivity/				Overall
(t-test)	AM background	TEM	EDX	Observations	likehood
< 0.05	≥2.0	<100 nm + agglomerates	Yes	Absence other sources	Likely
< 0.05	1.05–2.0	Agglomerates, few particles		Intrusion outdoor air	Possibly
>0.05	<1.05	Large particle agglomerates	Not	Other sources	Not likely

 Table 2.1
 Decision criteria to move to tier three in the exposure assessment Brouwer et al. [8]

AM arithmetic mean, TEM transmission electron microscopy, EDX energy dispersive X-Ray

the exposure but on an assessment of risk (i.e. the combination of the exposure and hazard). In tier one all the available information is used to make a decision about the likelihood of emission into the workplace atmosphere. The approach points to several tools that could be used for such assessment (e.g. MARINA exposure library, control banding tools). If the health risk is not considered to be negligible, the user moves to tier two, where the emission of ENM is confirmed through measurements (off-line particle characterization and chemical identification) [47].

The strategies described above do not provide a consistent framework for – reporting the measurements. Some recommendations and guidelines are given; e.g. Brouwer et al. [8] recommends that the results should be summarised into size bins of ≤ 100 nm and >100 nm. Other issues such as the number of measurements required to obtain a representative concentration, assessment of personal exposure and transport processes from the source to the receptor are not fully addressed in any of the proposed strategies.

2.2 Consumers Exposure

The development of nanotechnology has unleashed the manufacture of consumer products containing ENMs. The Woodrow Wilson inventory (http://www.nanotech-project.org/cpi/) currently lists 1,600 products in the market claiming to contain ENMs. The Nanowerk database (http://www.nanowerk.com/nanomaterial-database. php) has information on the characteristics and suppliers of 3,000 different types of ENMs. The types of products spread across a wide range of categories, from building materials, sport equipment, electronics and automotive materials, nanomedicine, to personal use products that are used/applied directly on the skin such as clothes, deodorant, cosmetics and sun creams as well as food and food-packing materials [30].

Figure 2.1 shows the estimated maximum volume (metric tons/year) of ENMs used in different product categories in 2010 based on a marker study from Future Markets [18].

While the ENMs are meant to increase the performance of the product, their presence in consumer products has raised concerns over their safety towards human health and the environment. Consumer exposure can occur through direct contact



Fig. 2.1 Estimated global volume production of ENM across product sectors (Based on Keller et al. [30])

from the use of products (e.g. sun creams, clothes) or indirectly through the environment (e.g. contact with water, air, soil contaminated with ENMs) or products contaminated with ENMs (e.g. ENMs leached from food packing). Therefore, consumers can be exposed through all exposure pathways (inhalation, dermal, ingestion and eyes). Children exposure through mouthing of materials should also be considered as well as any other susceptible exposed populations.

Several studies have attempted to understand the mechanisms of ENM release from consumers' products (NanoRelease: http://www.ilsi.org/ResearchFoundation/ RSIA/Pages/NanoRelease1.aspx: NanoHouse: http://www-nanohouse.cea.fr/: Scaffold: http://www.scaffold.eu-vri.eu/). These studies have provided very useful data on release to evaluate whether consumers can be potentially exposed through the environment; however, in most cases they do not provide quantitative exposure information. Within the NanoRelease project, exposure to consumers from sports equipment and electronics was estimated to be unlikely whilst exposure from tyres and textiles was found to be likely. Therefore, the magnitude of the release from consumer products will largely depend on the type of product, how much energy is applied to it (e.g. tires) and the presence of physical barriers between the ENMs and the consumers (e.g. electronics). The NanoHouse project concluded that for ENM used in paints under hard abrasion and leaching were mainly released embedded within a matrix or in agglomerate form. Very few single nanoparticles were released from paints. Pirela et al. [46] assessed consumers' exposures to particles release during laser printing using inks containing ENMs. The results showed that particles of silica, alumina, titania, iron oxide, zinc oxide, copper oxide, cerium oxide, carbon black among others could be released into the air during printing.

When assessing consumers' exposure it is important to know the conditions of use (specific use and exposure route, frequency, amount used per application), the form and characteristics of the ENM in contact with the human body and how the ENM migrates from the product to the body. ENMs are incorporated in different forms, suspended in liquids, suspended in solids, bound to the surface and embedded in a matrix [20]. It should be noted that the ENM released from the matrix might have different characteristics to the primary ENM incorporated into the manufactured product (e.g. coating may be removed) [42]. In order to understand the potential health effects and to develop acceptable daily intake levels it is important to be able to characterize these changes.

Modelling of consumers' exposure to ENM is less advanced than workers' exposure. Environmental flow dynamic models can predict the concentrations of ENM in different compartment levels providing therefore an insight on the potential indirect exposure to consumers. For example direct exposure to ENM in composites is considered to be unlikely. However, emissions to the environment at the end of life of the ENM are likely. Sun et al. [51] estimated annual emissions in 2014 in the EU to the surface water of 7,610 ton for nano-TiO₂, 1,330 ton for nano-ZnO and 1.27 ton CNT; for natural and urban soil of 2,230 ton for nano-TiO₂, 1,380 ton for nano-ZnO and 26.5 ton CNT; for sludge treated soil emissions were 45,400 for nano-TiO₂, 1.35 ton for nano-ZnO and 8.67 ton CNT and emission in the air of 324 ton for nano-TiO₂, 149 ton for nano-ZnO and 2.80 ton CNT.

Despite these studies and the existing consumer product inventories (e.g. Woodrow Wilson inventory; ANEC-BEUC 2010 inventory of consumer products containing nanomaterials; Wijnhoven et al. [58]), there are few quantitative data available on consumers' exposure.

Using the best estimates available and/or worst-case assumptions, Hansen et al. [21] estimated consumer exposure to be 26, 15, and 44 μ g/kg bw/year for a facial lotion, a fluid product, and a spray product containing nanoparticles, respectively. Chen et al. [14] estimated a mass of nano-TiO₂ in the breathing zone of 170 μ g/m³ during 2.5 min application of a bathroom cleaning propellant spray containing nano TiO₂.

The assessment of consumers' exposure to ENM is more challenging, as the materials contained in the products are not well characterized and are mixed with other chemicals that affect the release and transfer of the ENM and their availability for exposure. Further studies using standard protocols are required to better understand consumers' exposure.

2.3 Exposure During the End of Life

There is little information available on the potential for exposure to nanomaterialcontaining products during disposal and recycling stages. Established recycling schemes are available for consumer products such as electronics, packaging as well as large-scale dismantling of appliances, cars, aircraft and structures like wind turbine blades. Releases of ENM from the product matrix and exposure through endof-life processes are possible as they generally involve high energy, abrasive processes, e.g. incineration, shredding, cutting, bailing and storage in open space environments [7]. Further studies are required to better understand the release scenarios associated with end-of-life processes.

References

- Aitken RA, Bassan A, Friedrichs S, Hankin SM, Hansen SF, Holmqvist J, Peters SAK, Poland CA, Tran CL (2011) Specific advice on exposure assessment and hazard/risk characterisation for nanomaterials under REACH
- Asbach C, Kaminski H, Von Barany D, Kuhlbusch TAJ, Monz C, Dziurowitz N, Pelzer J, Berlin K, Dietrich S, Götz U, Kiesling HJ, Schierl R, Dahmann D (2012) Comparability of portable nanoparticle exposure monitors. Ann Occup Hyg 56:606–621
- Asbach C, Kuhlbusch, TAJ, Kaminski H, Stahlmecke B, Plitzko S, Götz U, Voetz M, Kiesling HJ, Dahmann D (2012) NanoGEM standard operation procedures for assessing exposure to nanomaterials, following a tiered approach
- Asbach C, Neumann V, Monz C, Dahmann D, van Tongeren M, Alexander C, MacCalman L, Todea AM (2017) On the effect of wearing personal nanoparticle monitors on the comparability of personal exposure measurements. Environ. Sci.: Nano, Advance Article, DOI: 10.1039/c6en00362a
- BAuA, BG RCI, IFA, IUTA, TUD, VCI (2011) Tiered approach to an exposure measurement and assessment of nanoscale aerosols released from engineered nanomaterials in workplace operations
- Bekker C, Kuijpers E, Brouwer DH, Vermeulen R, Fransman W (2015) Occupational exposure to nano-objects and their agglomerates and aggregates across various life cycle stages; A broad-scale exposure study. Ann Occup Hyg 59:681–704
- 7. Boldrin A, Hansen SF, Baun A, Hartmann NIB, Astrup TF (2014) Environmental exposure assessment framework for nanoparticles in solid waste. J Nanopart Res 16:2394
- Brouwer D, van Duuren-Stuurman B, Berges M, Jankowska E, Delphine B, Mark D (2009) From workplace air measurement results toward estimates of exposure? Development of strategy to assess exposure to manufactured nano-objects. J Nanopart Res 11:1867–1881
- Brouwer D, Berges M, Virji MA, Fransman W, Bello D, Hodson L, Gabriel S, Tielemans E (2012) Harmonization of measurement strategies for exposure to manufactured nano-objects; report of a workshop. Ann Occup Hyg 56:1–9
- Brouwer DH (2013) Workplace air measurements and likelihood of exposure to manufactured nano-objects, agglomerates, and aggregates. J Nanopart Res 15:2090
- Brouwer D, Boessen R, van Duuren-Stuurman B, Bard D, Moehlmann C, Bekker C, Fransman W, Entink RK (2016) Evaluation of Decision Rules in a Tiered Assessment of Inhalation Exposure to Nanomaterials. Ann Occup Hyg 60(8):949–959
- BSI (2010) Nanotechnologies—part 3: guide to assessing airborne exposure in occupational settings relevant to nanomaterials. British Standards Institution, London (BSI PD 6699-3:2010)
- European Committee for Standardisation (CEN) (1993) Workplace atmospheres size fraction definitions for measurement of airborne particles. Standard EN 481, Brussels
- 14. Chen BT, Afshari A, Stone S, Jackson M, Schwegler-Berry D, Frazer DG, Castranova V, Thomas AT (2010) Nanoparticles-containing spray can aerosol: characterization, exposure assessment, and generator design. Inhal Toxicol 22:1072–1082
- 15. Dahm MM, Evans DE, Schubauer-Berigan MK, Birch ME, Deddens JA (2013) Occupational exposure assessment in carbon nanotube and nanofiber primary and secondary manufacturers: mobile direct-reading sampling. Ann Occup Hyg 57:328–344
- Donalson K, Li XY, Macnee W (1998) Ultrafine (nanometer) particle mediated lung injury. Aerosol Science 29:553–560
- 17. Donaldson K, Murphy FA, Duffin R, Poland CA (2010) Asbestos, carbon nanotubes and the pleural mesothelium: a review of the hypothesis regarding the role of long fibre retention in the parietal pleura, inflammation and mesothelioma. Part Fibre Toxicol 7:5
- 18. Future Markets (2012) The global market for nanomaterials 2002–2006; production volumes, revenues and end use markets
- Guichard R, Tanière A, Belut E, Nimbert N (2014) Simulation of nanoparticle coagulation under Brownian motion and turbulence in a differential–algebraic framework: developments and applications. Int J Multiphase Flow 64:73–84
- Hansen SF, Michelson ES, Kamper A, Borling P, Stuer-Lauridsen F, Baun A (2008) Categorization framework to aid exposure assessment of nanomaterials in consumer products. Ecotoxicology 17:438–447

- 2 Assessment of Human Exposure to ENMs
- 21. Hansen SF (2010) Regulation and risk assessment of nanomaterials Too little, too late? PhD Thesis. Technical University of Denmark
- Hornsbya KE, Pryor SC (2014) A laboratory comparison of real-time measurement methods for 10–100-nm particle size distributions. Aerosol Sci Tech 58:571–582
- 23. IARC (2015) Carbon nanotubes (CNT), fluoro-edenite and silicon carbide, vol 111. WHO, International Agency for Research on Cancer
- 24. IFA (2009) Criteria for the assessment of the effectiveness of protective measures. Available at: http://www.dguv.de/ifa/Fachinfos/Nanopartikel-am-Arbeitsplatz/Beurteilung-von-Schutzma%C3%9Fnahmen/index-2.jsp. Last accessed: 25 Aug 2016
- ISO/TR 27628: 2007 Workplace atmospheres Ultrafine, nanoparticle and nano-structured aerosols – Inhalation exposure characterization and assessment. http://www.dguv.de/ifa/Fachinfos/ Nanopartikel-am-Arbeitsplatz/Beurteilung-von-Schutzma%C3%9Fnahmen/index-2.jsp
- 26. ISO 28439: 2011 Workplace atmospheres characterization of ultrafine aerosols/nanoaerosols – determination of the size distribution and number concentration using differential electrical mobility analysing systems
- 27. ISO/TR 1225: 2012 Nanomaterials-quantification of nano-object release from powders by generation of aerosols
- Jespersen TS, Nygård J (2007) Mapping of individual carbon nanotubes in polymer/nanotube composites using electrostatic force microscopy. Appl Phys Lett 90:183108
- 29. Kaminski H, Kuhlbusch TAJ, Rath S, Götz U, Sprenger M, Wels D, Polloczek J, Bachmann V, Dziurowitz N, Kiesling HJ, Schwiegelshohn A, Monz C, Dahmann D, Asbach C (2013) Comparability of mobility particle sizers and diffusion chargers. J Aerosol Sci 57:156–178
- Keller AA, McFerran S, Lazareva A, Suh S (2013) Global life cycle releases of engineered nanomaterials. J Nanopart Res 15:1692
- Klein Entik RH, Bekker C, Fransman W, Brouwer D (2015) Analysis of time series of particle size distributions in nano exposure assessment. J Aerosol Sci 81:62–69
- 32. Klein Entik RH, Fransman W, Brouwer D (2011) How to statistically analyse nano exposure measurement results: using an ARIMA time series approach. J Nanopart Res 123:6991–7004
- Koivisto AJ, Yu M, Hämeri K, Seipenbusch M (2012) Size resolved particle emission rates from an evolving indoor aerosol system. Aerosol Sci 47:58–69
- 34. Kuhlbusch TAJ, Asbach C, Fissan H, Göhler D, Stintz M (2011) Nanoparticle exposure at nanotechnology workplaces a review. Part Fibre Toxicol 8:22
- 35. Methner M, Hodson L, Geraci C (2010) Nanoparticle emission assessment technique (NEAT) for the identification and measurement of potential inhalation exposure to engineered nanomaterials – part A. J Occup Environ Hyg 7:127–132
- 36. Methner M, Hodson L, Geraci C (2010c) Nanoparticle emission assessment technique (NEAT) for the identification and measurement of potential inhalation exposure to engineered nanomaterials—Part B: results from 12 field studies. J Occup Environ Hyg 7:163–176
- 37. NIOSH (1994) Method 5040: elemental carbon (diesel particulate) method. NIOSH manual of analytical methods, 4th edn. NIOSH, Cincinnati, OH. DHHS (NIOSH)
- 38. NIOSH (1998) Method 0600: particulates not otherwise regulated (respirable) NIOSH manual of analytical methods, 4th edn. NIOSH, Cincinnati, OH. DHHS (NIOSH)
- NIOSH (2003) Method 7300: elements by ICP. NIOSH manual of analytical methods, 4th edn. NIOSH, Cincinnati, OH. DHHS (NIOSH)
- 40. NIOSH (2011) Current intelligence bulletin 63: occupational exposure to titanium dioxide. U.S. Department of Health and Human Services, Centers for Disease Control, National Institute for Occupational Safety and Health. DHHS (NIOSH) Publication No. 2011–160, Cincinnati
- 41. NIOSH (2013) Current intelligence bulletin 65: occupational exposure to carbon nanotubes and nanofibers. Cincinnati, OH: U.S. Department of Health and Human Services, Centers for Disease Control, National Institute for Occupational Safety and Health. DHHS (NIOSH) Publication No. 2013–145
- 42. Nowack B, Ranville JF, Diamond S, Gallego-Urrea JA, Metcalfe C, Rose J, Horne N, Koelmans AA, Klaine SJ (2012) Potential scenarios for nanomaterial release and subsequent alteration in the environment. Environ Toxicol Chem 31:50–59
- 43. OECD (2015) Harmonized tiered approach to measure and assess the potential exposure to airborne emissions of engineered nano-objects and their agglomerates and aggregates at work-

places. OECD Health and Safety Publications. Series on the Safety of Manufactured Nanomaterials. No.55. ENV/JM/MONO(2015)19

- 44. Oberdörster G (1996) Significance of particle parameters in the evaluation of dose-response relationships of inhaled particles. Inhal Toxicol 8 Suppl:73–89
- 45. Peters TM, Elzey S, Johnson R, Park H, Grassian VH, Maher T, O'Shaughnessy P (2009) Airborne monitoring to distinguish engineered nanomaterials from incidental particles for environmental health and safety. J Occup Environ Hyg 6:73–81
- 46. Pirela SV, Sotiriou GA, Bello D, Shafer M, Bunker KL, Castranova V, Thomas T, Demokritou P (2014) Consumer exposures to laser printer-emitted engineered nanoparticles: a case study of life-cycle implications from nano-enabled products. Nanotoxicology 11:1–9
- 47. Schinwald A, Murphy FA, Jones A, MacNee W, Donaldson K (2012) Graphene-based nanoplatelets: a new risk to the respiratory system as a consequence of their unusual aerodynamic properties. ACS Nano 6:736–746
- 48. Schneider T, Brouwer DH, Koponen IK, Jensen KA, Fransman W, Van Duuren-Stuurman B, Van Tongeren M, Tielemans E (2011) Conceptual model for assessment of inhalation exposure to manufactured nanoparticles. J Expo Sci Environ Epidemiol 21:450–463
- 49. Seipenbusch M, Binder A, Kasper G (2008) Temporal evolution of nanoparticle aerosols in workplace exposure. Ann Occup Hyg 52:707–716
- 50. Silva RM, Xu J, Saiki C, Anderson DS, Franzi LM, Vulpe CD, Gilbert B, Van Winkle LS, Pinkerton KE (2014) Short versus long silver nanowires: a comparison of in vivo pulmonary effects post instillation. Part Fibre Toxicol 11:52
- Sun TY, Bornhöft NA, Hungerbühler K, Nowack B (2016) Dynamic Probabilistic Modeling of Environmental Emissions of Engineered Nanomaterials. Environ. Sci. Technol., 50:4701–4711
- 52. Van Broekhuizen P, Van Broekhuizen F, Cornelissen R, Reijnders L (2012) Workplace exposure to nanoparticles and the application of provisional nanoreference values in times of uncertain risks. J Nanopart Res 14:770
- 53. Mills JB, Parka JH, Petersa TM (2014) Comparison of the DiSCmini aerosol monitor to a handheld condensation particle counter and a scanning mobility particle sizer for submicrometer sodium chloride and metal aerosols. J Occup Environ Hyg 10:250–258
- 54. Murphy FA, Poland CA, Duffin R, Al-Jamal KT, Ali-Boucetta H, Nunes A, Byrne F et al (2011) Length-dependent retention of carbon nanotubes in the pleural space of mice initiates sustained inflammation and progressive fibrosis on the parietal pleura. Am J Pathol 178:2587–2600
- 55. UK NanoSafety Partnership Group (UKNSPG) 20120 Working Safely with Nanomaterials in Research & Development
- Verma NK, Moore E, Blau W, Volkov Y, Babu PR (2012) Cytotoxicity evaluation of nanoclays in human epithelial cell line A549 using high content screening and real-time impedance analysis. J Nanopart Res 14:1137
- 57. Witschger O, Le-Bihan O, Reynier M, Durand C, Charpentier D (2012) Préconisation en matière de caractérisation et d'exposition des potentiels d'emission et d'exposition professionnelle aux aerosols lors d'operations nanomateriaux, INRS – Hygiène et sécurité du travail – 1er trimester 2012, 226:41–55
- Wijnhoven WEP, Oomen Ir AJ, Sips AJAM, Bourgeois FC, Dorsthorst GJPM te, Kooi MW, Bakker MI (2010) Development of an inventory for consumer products containing nanomaterials. DG Environment within the framework of ENV/D3/SER/2010/0060r
- Zhao M, Gu X, Lowther SE, Park C, Jean YC, Nguyen T (2010) Subsurface characterization of carbon nanotubes in polymer composites via quantitative electric force microscopy. Nanotechnology, 20;21(33):339801