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TECHNISCHE UNIVERSITÄT DRESDEN

Tiered Approach to an Exposure Measurement and Assessment of Nanoscale Aerosols Released from Engineered Nanomaterials in Workplace Operations

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Tiered Approach to an Exposure Measurement and Assessment of Nanoscale Aerosols Released from Engineered Nanomaterials in Workplace Operations

presented by: [1] Air Quality and Sustainable Nanotechnology, Institute of Energy and Environmental Technology e.V. (IUTA) Federal Institute for Occupational Safety and Health (BAuA) German Social Accident Insurance Institution for the Raw Materials and Chemical Industry (BG RCI) German Chemical Industry Association (VCI) Institute for Occupational Safety and Health of the DGUV (IFA) Research Group Mechanical Process Engineering, Institute of Process Engineering and Environmental Technology, Technical University Dresden (TUD)
[1] in alphabetical order

Germany, August 2011

1 Executive Summary

Engineered nanomaterials (ENMs) are often fascinating, new materials with significantly improved or completely novel properties [BIAC]. Some other ENMs are materials, which have been marketed for decades, e.g., carbon black, synthetic amorphous silica, pigments, etc. are or may also be affected by the nanotechnology debate. They are being handled in the workplaces both in research and in production. The Chemical Industry in Germany has subscribed to the Responsible Care Global Charter and is therefore committed to a safe, responsible and sustainable development of this highly promising technology. This includes appropriate organizational measures as well as the implementation of a high level of industrial hygiene standards. Amongst others, it has lead to the development of the Guidelines on the Responsible Use of Nanomaterials in the Workplace, jointly issued by BAuA and VCI in 2007 [BAua, VCI], [Heinemann]. The German Social Accident Insurance (DGUV) has also committed itself to support the responsible use of nanomaterials [IFA 1]

Industrial hygienists are interested in the measurement and management of the exposure to the inhalable and respirable dust fraction, including the nanoscale fraction [Dust Fraction], [DIN EN 1]. The tiered approach and thus the present document focuses on a size range from 1 nm to 100 nm and is designed to support assessment of health risks from solid, particulate substances released as nanoscale aerosol from ENMs in routine workplace operations. Therefore, aerosols containing nano-objects and their nanoscale aggregates and agglomerates are targeted by this approach. Efficient, reliable, but also pragmatic exposure assessment is a crucial element and the starting point for the effective management of risks potentially posed by hazardous chemicals in the workplace.

Therefore, the Institute of Energy and Environmental Technology e.V. (IUTA), the Federal Institute for Occupational Safety and Health (BAuA), the German Social Accident Insurance Institution for the Raw Materials and Chemical Industry (BG RCI), the Institute for Occupational Safety and Health of the DGUV (IFA), the Technical University Dresden (TUD) and the German Chemical Industry Association (VCI) established a working group to address and discuss the challenges of exposure measurement and assessment[2] of nanoscale aerosols released from ENMs in the workplace.[3] The working group aimed at a harmonized approach towards such exposure measurement. The outcome was designed to be pragmatic and widely usable, rather than to form the basis for further scientific and research oriented studies. A tiered approach is the result, which can be widely used by small and medium size enterprises as well as large chemical companies with global business operations.

THE MAIN FINDINGS OF THE WORKING GROUP CAN BE SUMMARIZED AS FOLLOWS:

- Safe work places where ENMs are produced or processed can be achieved, using existing technology, and which conforms with best industrial hygiene practices. Existing substance-specific, binding, health based OELs must be complied with and are not subject of or overridden by the current approach.
- Exposure measurement of nanoscale aerosols released from ENMs in the work-place is possible and exposure assessment methodologies exist. However, methodologies are not yet standardized and more difficult to apply as in routine operations, e.g. gravimetric dust measurements according to DIN EN 481.
- Equipment required for measurement of exposure to nanoscale aerosols released from ENMs is sophisticated and the results produced, e.g., total particle number concentration, have no direct correlation to the chemical identity. Calibration of equipment is still a challenge and validation using round robin testing, which is typically correlated with SMPS results, is difficult as no commonly accepted reference method is available.
- At the moment, for a practitioner, a tiered approach to exposure assessment appears to be the most appropriate strategy. This approach is split into 3 tiers. In the first step (Tier 1) information is gathered according to established industrial hygiene practices. In the next tier (Tier 2) a basic exposure assessment using a limited set of easy-to-use equipment is conducted, where as in the highest tier 6 (Tier 3) the latest state-of-the-art measurement technology is employed to assess the potential for workplace exposure to nanoscale aerosols released from ENMs if required.
- Existing legally binding OELs, e.g. synthetic amorphous silica [TRGS 900: EC No. 231-545-4], carbon black [ACGIH], etc., have to be complied with. Where no such substance-specific, binding, health-based OEL values for ENMs exist, the tiered approach is using 3 criteria for the assessment of the data:
1) Interference value exceeded for nanoscale aerosols released from ENMs.
2) Significant increase over aerosol background level in the workplace air.
3) Chemical identity of the nano-objects and their nanoscale aggregates and agglomerates detected in the aerosol.
- The application of the decision logic leads in total to 7 different cases (Case A – G), which may guide the risk management decisions of the practitioner.
- This step-by-step approach may need to be revisited as soon as new scientific findings are available (especially on binding, health-based occupational exposure limit values). The presented exposure assessment strategy of nanoscale aerosols released from ENMs in the workplace may serve as a starting point for further standardization.

[2] Exposure measurement and assessment are an integral element in the overall risk assessment in the workplace.
[3] The presented approach considers permanently situated workplaces, e.g., in a production facility. Varying assignments, e.g., as typical in the construction industry are less in its focus.

2 Drivers and Specific Challenges

ENMs are being handled more and more in workplaces, both in research and in production, as a wide range of different ENMs are used to develop and produce new structures, materials and devices.

Currently only a few substance-specific, health-based exposure limits for ENMs in workplace operations have been proposed [NIOSH 1], [Pauluhn 1 and 2], [Schulte]. Even though OECD test protocols are applicable for ENMs [OECD 1], uncertainties concerning the hazards and risks potentially posed by ENMs exist. Exposure assessment and control become thus even more important. Therefore, an urgent need exists for reliable exposure measurement and assessment of aerosols containing ENMs in workplace operations.

As long as the field of toxicology of ENMs is evolving and no substance-specific, binding, health-based OELs have been established and validated, control of ex-posure in the workplace has to adequately protect the workforce.

Efforts have been undertaken thus far by various organizations and initiatives[4], to tackle the issue of workplace air emissions and exposure measurement by monitoring potentially affected workplaces and starting to harmonize the required protocols.

The focus of these initiatives was either tailored to a project [NANOCARE] or more research oriented [TNO], whereas a pragmatic approach, which could be easily applied by and thus widely applicable to the practitioner in the field, was missing and therefore is in the focus of this joint initiative to present a tiered approach.

Internationally active organizations and companies, who are involved in the development of innovative materials including ENMs with novel and superior properties, develop, produce and use materials containing ENMs worldwide. The current approach is an example for an initiative of the Institute of Energy and Environmental Technology e.V. (IUTA), the Federal Institute for Occupational Safety and Health (BAuA), the German Social Accident Insurance Institution for the Raw Materials and Chemical Industry (BG RCI), the Institute for Occupational Safety and Health of the DGUV (IFA), the Technical University Dresden (TUD) and the German Chemical Industry Association (VCI) aiming to produce coherent industrial hygiene including an exposure assessment strategy and methodologies to enable effective and efficient decisions for the management of risks during the production and handling of ENMs. The presented approach, which could be used for routine exposure measurement and assessment in the field, may also be beneficial for small and medium enterprises (SMEs), for down-stream users in non-chemical industries and consultants for occupational safety, which may be less experienced in exposure assessment of nanoscale aerosols released from ENMs in workplace operations.

A tiered approach to the exposure assessment of nanoscale aerosols released from ENMs in workplace operations is deemed most effective. Its main advantage is the most efficient use of limited, qualified resources to ensure a high level of protection of the workforce.

[4] e.g., the German BMBF project NANOCARE [NANOCARE], the EU project NANOSH [NANOSH], OECD [OECD 2], NIOSH [Methner] as well as TNO, PEROSH and IFA [TNO]

3 Scope of the Document

Industrial hygienists are interested in the assessment of the exposure to the inhalable and respirable dust fraction, including the nanoscale fraction. [Dust Fraction], [DIN EN 1] The tiered approach and thus the present document focuses on a size range from 1 nm to 100 nm and is supposed to support exposure assessment of solid, particulate substances released as aerosol from ENMs in routine workplace operations. Therefore, nanoscale aerosols containing nano-objects and their nano-scale aggregates and agglomerates are targeted by this approach, which is complementary to established exposure measurement methodologies for the inhalable and respirable dust fraction above this size range.

THIS APPROACH …

- … does not apply to cases of non-routine release of nanoscale aerosols released from ENMs, e.g., spills and other incidents. In such cases, appro-priate exposure mitigation measures shall be taken in accordance with specific site procedures.
- … is applicable both in commercial production operations and R&D laboratories and pilot plants.

The approach and the methodologies are not supposed to substitute existing ex-posure measurement and assessment strategies for the inhalable or respirable fraction of non-nanoscale particulates that are measured in accordance with estab-lished regulatory requirements, company or other organizations' protocols [Dust Fraction].

3.1 Definition of the Phrase Engineered Nanomaterial and Nanoscale Aerosols Released from ENMs as used in this Document

ENMs that are in the focus of this document are particulates dispersed in workplace air. Such ENMs could contain nano-objects and their nanoscale aggregates and agglomerates. For the purpose of the document and the simplicity of the reading this is called „nanoscale aerosols released from ENMs".

A scientific definition has been established by ISO/TC229…

- … nano-objects are discrete particles with one, two or three external di-mensions between approximately 1 nm and 100 nm according to ISO TS 27687:2008 [ISO 1].
- … nanostructured materials comprise, amongst others, aggregates and agglo-merates of nano-objects according to ISO DTS 80004-4 [ISO 2].

Nano-objects and nanostructured materials represent subcategories of the generic term nanomaterial according to ISO TS 27687:2008.

Apart from the above ISO definitions, a number of organizations, in various contexts, have also proposed definitions of engineered nanomaterials, primarily for regulatory purposes, e.g., VCI [VCI 1], ACC [ACC], EC, JRC [JRC], SCENIHR, [SCENIHR] etc. Contrary to the ISO approach, all of these definition proposals use quantitative criteria that are indispensable when conducting an industrial hygiene exposure assessment. The International Council of Chemical Associations (ICCA), for instance, has published a proposal for a Regulatory Definition of Nanomaterials [ICCA] in December 2010.

Assessment of data produced for industrial hygiene purposes requires a definite upper limit for the nanoscale. Thus, for the purpose of this document and the tiered approach presented herein, and guided by ISO [ISO 1][5], „nanoscale" is defined as the size range from 1 nm to 100 nm. In practice there are limitations because the measurement ranges of most of the available devices are not specifically aligned with the nanoscale fraction of aerosols. However, it is good industrial hygiene practice, to include the inhalable[6] and respirable[7], [8] objects above 100 nm in the measurement [Mattenklott]. This will capture all aggregates or agglomerates of nano-objects.

The document may have to be revised as soon as a mandatory, regulatory definition of engineered nanomaterials has been adopted.

3.2 Identification of ENMs - Examples

Substances, which under industrial hygiene aspects may currently qualify as ENMs based on the indicators described below (the latter may change over time) are…

- … intentionally manufactured and have at least one dimension at or below 100 nm. Naturally occurring nanomaterials or incidental nanoscale materials, e.g., combustion by-products are excluded.
- … listed in the testing program for ENMs of the Organization of Economic Cooperation and Development (OECD) (compare annex 2).
- … produced or delivered as being an ENM according to the MSDS [VCI 2] or alternative information sources, e.g., Technical Information Sheets, etc.
- … solid, and handling may create dust consisting of nanoscale airborne particu-lates.
- … having a fraction of more than 10 wt.-% below 100 nm according to their particle size distribution [ICCA] according to ICCA (compare chapter 2).
- … containing more than 50 wt.-% aggregates or agglomerates larger than 100 nm consisting of nano-objects [ICCA] according to ICCA (compare chapter 2).

There might be additional criteria that are decisive for defining substances to qualify as ENMs under industrial hygiene aspects, such as, for instance volume specific surface area above 1 × 6/100 nm [SCENIHR] (compare chapter 2).

3.3 Identification of Potential ENM Release Scenarios – Examples

Examples of scenarios that may lead to emission of nanoscale aerosols released from ENMs from workplace operations are:

- Production, handling or use of solid (e.g. dry powder), dusting [ISO 4] or airborne ENMs,
- Abrasive machining of materials containing ENMs (e.g., chipping, grinding [Göhler], [Koponen], etc.),
- Processes that are not completely contained,
- Interfaces between contained and open process steps (e.g., loading and un-loading, sampling),
- Waste disposal,
- Re-suspension of particulates from surfaces, e.g., from external housing of HEPA vacuum cleaners contaminated with particles or fibres (nano- and microscale)

or

- Cleaning, maintenance and over-hauling of process equipment and operation facilities. A system, which is completely contained [Directive 1] is designed to prevent nano-scale aerosols released from ENMs from escaping during normal operations. Inhalation and dermal exposure does normally not occur. Maintenance operations have to be assessed separately. This can be accomplished either by a complete enclosure of the nanoscale aerosols released from ENMs or an enclosure with openings with integrated highly efficient ventilation.

A closed laboratory fume hood according to DIN EN 14175 [DIN EN 2] can also be considered as a completely contained system as per own measurements and experiences.

5 under revision: ISO/NP TS 80004-2:2011 Nanotechnologies - Vocabulary - Part 2: Nano-objects: Nanoparticle, Nanofibre and Nanoplate

6 inhalable (= thoracic) dust fraction: mean aerodynamic diameter about 10 μm according to the US Department of Labor [US Labor] http://www.osha.gov/SLTC/silicacrystalline/dust/chapter_1.html

7 respirable dust fraction: mean aerodynamic diameter a.) < 5 μm according to the Johannesburg Convention, b.) mean aerodynamic diameter < 4 μm according to DIN EN 481 [DIN EN 1]

8 Size fractions of airborne dust are described in ISO7708, 1995.

3.4 Characteristics of Potentially Comparable Workplaces, Operations and Tasks

If workplaces, operations and/or tasks are comparable, read-across or bridging from existing exposure assessment data may also be considered in the decision process.

Workplaces, operations and/or tasks in one premise may be considered comparable, if all of the following applies:

- … identical or comparable (e.g., dustiness) materials are handled and the quantities are similar,
- … similar process technology and process equipment is used,
- … comparable containment and control measures are applied,
- … workplaces express similar air stream conditions (technical ventilation, air exchangerate),
- … similar safe handling practices are in place and
- … the workforce is adequately trained and instructed.

However, even in these cases it is recommended to proceed with caution and be aware to manage any changes which may occur over time.

4 Crucial Elements for the Applicability of the Tiered Approach in Practice

The present approach to an exposure assessment of nanoscale aerosols releasedfrom ENMs in the workplace is split into 3 tiers:

- Tier 1: Information gathering conducted according to established best practices in industrial hygiene
- Tier 2: Basic exposure assessment using a limited set of easy-to-use equipment
- Tier 3: Expert exposure assessment applying latest knowledge and technology. Measuring methods to be utilized and remarks on specific measurement strategies are given in chapter 4. The tiered approach is depicted in flowchart 1.

4.1 Tier 1: Information Gathering

At Tier 1 a decision has to be made, whether or not a release of nanoscale aerosols from ENMs into workplace air can be reasonably excluded. Preparing for this decision, it has to be investigated if ENMs are present in the workplace and if nanoscale aerosols from ENMs can be released into workplace air. Such investigation has to be undertaken as a risk assessment in the workplace in accordance with applicable law, e.g. Directive 98/24 EC [Directive 2], and has to be completed prior to the commencement of operations (see Chapters 3.2 to 3.4).

If the release of nanoscale aerosols released from ENMs can not be reasonably excluded the potential exposure must be assessed as per Tier 2.

4.2 Tier 2: Basic Exposure Assessment

Where substance-specific, binding, health-based OELs for ENMs are not available, the measurement results must be assessed on the basis of the interference value against the aerosol background level (see chapter 4.5).

If the interference value is exceeded and a significant increase over total aerosol background concentration is detected, then the potential exposure has to be investigated according to Tier 3 (Expert Exposure Assessment).

4.3 Tier 3: Expert Exposure Assessment

At Tier 3 the latest knowledge and measurement technology must be used to assess the potential workplace exposure to nanoscale aerosols released from ENMs.

Measurement equipment such as CPC, SMPS, NSAM or Aerosol Spectrometer is suggested as suitable for conducting an exposure assessment (see chapter 5). In parallel, sampling systems are employed to collect specimens for subsequent off-line analyses such as SEM, TEM or ICP-AES. For this purpose SOPs for the usage of the devices in the workplace should be followed. Protocols for the development of SOPs have been published, e.g., by NANOCARE.

If

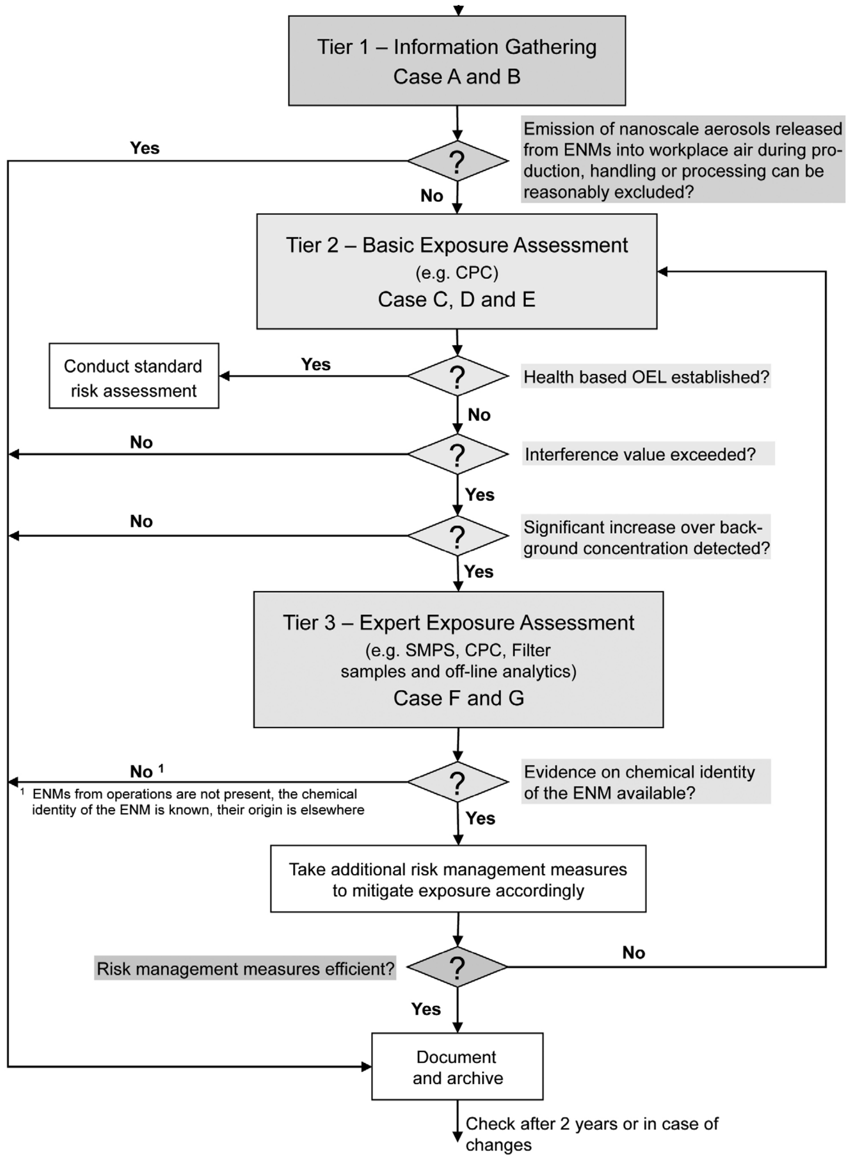
- nanoscale aerosols are released in the workplace,
- the interference value is exceeded,
- a significant increase over total aerosol background concentration is detected

and

- evidence is available for the chemical identity of the filter samples indicating that the source is the ENM,

exposure mitigation measures must be taken and their efficiency has to be proven using, at least, Tier 2 methodologies.

Based on in-depth process knowledge and past experience with the challenges and the feasibility of effective and efficient exposure mitigation measures, exposure reduction may already be useful at the respective tier employed, i.e. before moving to the higher tier and thus more sophisticated and expensive exposure measurement methodology.



Flowchart 1:
Decision Tree according to the Presented Tiered Approach

4.4 Additional Considerations

There may be complementary methods for assessing contamination in the workplace, e.g., wipe samples, sampling in Petri dishes, which are situated around the potentialemission source, etc. Results from these methods may be indicators for potential exposure to ENMs. These methods are not in the scope of the present document, as they are still on an exploratory stage and thus typically not standardized. Nonetheless, under particular circumstances, they may provide additional information forassessing the workplace situation.

4.5 Criteria for Assessment

Should substance-specific, binding health-based OEL values for the ENM be available they have, of course, to be met according to established protocols. Only if no such OELs are available it is proposed that three pragmatic criteria are used for the assessment of the exposure data. From an industrial hygiene perspective, these criteria represent the current analytical limitations and need to be holistically assessed:

1) Interference value exceeded for nanoscale aerosols released from ENMs.
2) Significant increase over aerosol background level in the workplace air.
3) Chemical identity of the airborne nano-objects and their nanoscale aggregates and agglomerates confirmed as that of the ENM.

The assessment thereof forms the basis for the decision on required risk management measures.

4.5.1 Interference Value

The interference value should represent the lowest value, which can be measured with sufficient reliability regardless of the applied metrics and based on the current limitations of the available methodologies and validation protocols. It is the starting point for the assessment of a potential exposure of personnel in a particular workplace. In addition to the interference value the significant increase over the aerosol background level in the workplace air has to be considered as another criterion.

The interference value is not health-based and is not intended to be used for deriving a binding or regulatory threshold limit value in the context of this document. However, it has to be established by the employer and it must be scientifically defendable.

Only a few OELs for individual nanoscale substances have already been proposed in literature, presentations or online, e.g., for „sub-pigmentary“ titanium dioxide [NIOSH 2] or MWCNTs [Pauluhn 2], [BSI].

Some organizations have also suggested threshold values for certain nanoscalematerials [Pauluhn 1], [BSI], [IFA], [Nanocyl], [OECD 3]. For example …

- … the National Institute of Occupational Safety and Health (NIOSH) recommended an exposure level of < 0.1 mg/m3 for ultrafine titania [NIOSH 2].
- … British Standards Institute (BSI) suggested a benchmark exposure level of 10.000 fibres/m^3 for MWCNTs based on total fibre concentration, which represents the binding OEL for asbestos in the UK [BSI].
- … Bayer HealthCare proposed a unifying denominator for poorly soluble particles for DNEL estimation with a volume-based generic mass concentration independent on „nano- or submicron-sized“ properties, as a generic no-adverse effect level in both rats and humans. This mass concentration was defined as 0.5 µl particulate matter (respirable) / m^3 × agglomerate density. [Pauluhn 1].
- … the National Institute of Occupational Safety and Health (NIOSH) published a Draft Current Intelligence Bulletin on Occupational Exposure to Carbon Nanotubes and Nanofibers [NIOSH 1]. NIOSH is proposing an exposure level of up to 7 µg/m^3 for elemental carbon as an average shift value accordingly. This value also represents the current level of quantification (LOQ) according to the NIOSH Method 5040 [NIOSH 3].
- … The Institute for Occupational Safety and Health of the DGUV (IFA) has recommended benchmark levels of 20.000 (for a density > 6.000 kg/m^3) or 40.000 particles/cm^3 (for a density < 6.000 kg/m^3) for biopersistent granular ENMs as increase over the aerosol background as average shift values [IFA 2].

The proposals are very diverse. They are expressed in different metrics (mass, volume as well as particle and fiber number concentration). Some were derived from toxicological studies by applying assessment factors, some are non-health based limits.

4.5.2 Significant Increase over Aerosol Background Level (Assessmentof the Aerosol Background, see chapter 4.2)

The measurement of nanoscale aerosols released from ENMs will always be a challenge due to the ubiquitous aerosol background level, which may mask an ENM release into workplace air. Typically, the aerosol background level is not constant but can vary substantially, depending on confounding release sources [Kuhlbusch 1 and 2] and on environmental and climatic conditions, e.g., airborne sea salt or soil particulates, external incineration and combustion sources, e.g., off-gas from muffles or flares the technical ventilation situation, humidity, etc. A significant increase over the aerosol background level [NANOCARE], [OECD 2], [Methner], [TNO], [NANOTRANSPORT] is thus required to assess nanoscale aerosols released from ENMs from a specific workplace operation. What would qualify as a significant increase is equipment and data quality based and mainly dependent on the statistical validity of measurements, which is based on the number of available data sets. Furthermore, sufficient contextual information is required to correlate the data to single confounding events. A significant increase of the aerosol background level needs to be addressed by the individual risk management protocols of the organizations.

The distinction from the aerosol background level will be discussed in chapter 5.2.

4.5.3 Composition and Chemical Identity of the Workplace Aerosol

In addition to the total amount of dust in the air, the chemical identity of the detected nanoscale objects should be assessed as a third criterion. For example the chemical identity may be identified by electron microscopy or atomic absorption spectroscopy of filter samples from workplace air.

4.6 Metrics

The discussion on the appropriate metric for exposure assessment of nanoscale aerosols released from ENMs in the workplace is still ongoing.

Typically the inhalable and respirable dust fraction is measured using mass concentration employing established protocols for the gravimetric determination of filter samples [Dust Fraction]. The inhalable dust fraction includes airborne particles with an aerodynamic diameter (AD) smaller than about 100 μm, the thoracic fraction captures particles with an AD of smaller than about 10 μm and the fraction with an AD smaller than about 4 μm is addressed as the respirable dust fraction according to DIN EN 481 [DIN EN 1]. The deposition of inhaled objects in the respiratory tract varies on their aerodynamic diameter [DIN ISO 1]. Both fractions may also contain nano-objects as well as aggregates and agglomerates comprising of nano-objects. However, the contribution of nano-objects to the total mass of the filter sample is usually negligible. The results based on mass concentration may thus serve as a starting point for measurement of exposure, but are typically considered insufficient to adequately characterize exposure to nanoscale aerosols released from ENMs. It is still uncertain and discussed in the Competent Authority Sub-Group Nano (CASG Nano)[9], if the total particle number concentration or the surface area concentration is the better exposure descriptor than mass concentration. For biological matrices a mass-based concentration is preferred in order to derive toxicological conclusions, although in that respect the surface-based metric is deemed to be of value, while particle concentration is considered of interest. [10] In practice, though, industrial hygienists measure preferentially particle number concentration as a more sensitive metric [Kuhlbusch 3] in addition to mass concentration to characterize exposure to nanoscale aerosols released from ENMs.

However, the decision logic as outlined in the following chapter will be applicable regardless of the applied metrics.

4.7 Decision Logic and Introduction of the Cases A – G

If it is known from literature or experimental data that the considered ENMs do not pose a health hazard but that, however, the process is not completely contained, measurements should be taken on the respirable dust fraction and an exposure assessment should be conducted according to Tier 2. If applicable substancespecific OELs are not exceeded, further exposure control measures are unlikely to be required.

The decision logic is not suitable, however, if the aerosol background level is significantly affected by confounding variables, for example by thermal processes and the interference value may thus be exceeded without any ENM operations.

The Tier 1 considerations and the decision logic, based on total particle number concentration, lead in total to 7 cases (Case A – G), which are summarized in table [1].

However, exposure mitigation measures must be taken,
• … if Case G (worst case) was identified (compare Table 1 and 2), i.e.:
1. The interference value is exceeded and
2. a significant increase over the aerosol background has been detected and
3. the chemical identity of the airborne particulate has been identified as the ENM handled in the operation.
• … in the case of ENMs that are regulated as WHO fibers or CMRs.

Table 1: Cases A – G according to the Tier 1 Considerations and the Decision Logic

Case	Tier	Interference value exceeded?	Significant increase over aerosol background detected?	Evidence on the chemical identity of the ENM used at the workplace in the aerosol?
A	1	Decision criteria not applicable: Nanoscale aerosols realeased from ENMs emission can be excluded.		
B	1	Decision criteria not applicable: Nanoscale aerosols realeased from ENMs emission can not be excluded. Proceed to Tier 2.		
C	2	No	No	No, typically not conducted in Tier 2.
D[1)]	2	No	Yes	No, typically not conducted in Tier 2.
E	2	Yes	No	No, typically not conducted in Tier 2.
F	3	Yes	Yes	No
G	3	Yes	Yes	Yes

[9] The Competent Authority Subgroup Nano (CASG Nano) is the CARACAL working group on nanomaterials, composed of representatives of the European member states and experts from various stakeholders. CARACAL is formed by the European competent authorities for REACH and CLP. CARACAL is an expert group, which advises the EC and the European Chemicals Agency (ECHA) on questions related to the REACH and CLP regulation.
[10] Discussed within RIP-oN 2 and 3.fractions of airborne dust are described in ISO7708, 1995.

Table 2: Measures according to the Identified Cases A – G

Case	Tier	Measures
A	1	Document and archive.
B	1	Document and archive. Proceed to Tier 2.
C	2	Document and archive. Additional exposure mitigation measures are optional
D	2	Document and archive. Increase the frequency of workplace monitoring. (Additional exposure mitigation measures may not be required, if the chemical identity can be identified as ubiquitous aerosol background level.)
E	2	Document and archive. Proceed to Tier 3.
F	3	Document and archive. Based on contextual information decision has to be made, if additional exposure mitigation measures are not required.
G	3	Document and archive. Take appropriate exposure mitigation measures. Check efficiency of the measures once implemented.

5 Suitable Measurement Equipment for Tier 2 and 3 Exposure Measurement

The following measurement equipment [Pelzer] is suggested as suitable for use in exposure measurements. Other equipment may be equivalent and appropriate to establish an effective aerosol measurement, characterization and interpretation for risk mitigation.

5.1 Measurement Equipment [Kuhlbusch 3]

5.1.1 Suitable Measurement Equipment for Tier 2

Direct Reading, Counting Devices:

• Condensation Particle Counter (CPC), measurement range: lower limit typically below 20 nm, upper limit 350 -1 000 nm.

• Nanoparticle monitors using electrical detection principle, lower limit typically 25 nm, upper limit up to 350 nmon and interpretation for risk mitigation.

5.1.2 Suitable Measurement Equipment for Tier 3

Direct Reading, Counting Devices:

• Condensation Particle Counter (CPC), measurement range: lower limit typically below 10 nm, upper limit approximately 1 000 nm
• Scanning Mobility Particle Sizer (SMPS), measure ment range: lower limit typically below 10 nm, upper limit 350 – 1 000 nm
• Fast Mobility Particle Sizer (FMPS), measurement range: lower limit typically 6 mn, upper limit 560 nm
Counting and Sampling Devices:
• Electrostatic sampler, e.g. Nanometer Aerosol Sampler (e.g. NAS, TSI),
• Electrostatic and Thermal Precipitator (e.g. Model 5.561, Grimm)
• Filtration Sampler using grids for electron microscopy as collection medium (Filtration Sampler, e.g. VTT)
• Filtration Sampler using gold coated membrane filters Filter samples can be analyzed by Atomic Emission Spectroscopy (ICP-AES), Scanning Electron Microscopy (SEM) or Transmission Electron Microscopy (TEM.)

5.2 Assessment of and Distinction of Nanoscale Aerosol from Aerosol Background Level and other Spatial and Temporal Aerosol Contributors

If an ENM specific measurement is not possible with state-of-the art equipment, the distinction from the aerosol background level is crucial for valid exposure assessment. Typically this is accomplished by conducting comparative measurements. After defining the activity or relevant operation to be addressed, the distinction from aerosol background can basically be accomplished

- by measurements before and after operations (e.g., a suggested sequence to sampling: 1) without equipment on, 2) with equipment on 3) with handling of ENM 4) after the operation and clean-up completed, no handling of ENM, with equipment on and then without equipment on (see chapter 5.2.1) or
- by simultaneous measurements close to and far from the concerned work area (near- and far-field measurements) during operations, e.g., inside and outside of the operation plant

In addition, it is recommended to record climatic data, especially temperature and atmospheric humidity. If technically feasible it is also advisable to measure and document the wind/air stream conditions.

Furthermore any activities, for example traffic, electric motors, etc. in the relevant work area need to be documented for identification of confounding variables.

5.2.1 Activity-Based Analysis and Measurements for Tier 2 and 3

Experience has shown that air sampling measurements are always impacted by both nanoscale aerosols released from ENMs stemming from the monitored activity or operation and by nanoscale aerosols generated by surrounding activities, e.g., forklift truck exhaust. In order to identify the relevant ENM exposure potential resulting from the activity or operation and to exclude other impacts, it is important to correlate the respective contributions with the measurement result by taking into account all spatio-temporal contributions.

In conjunction with the exposure measurement an activity-based analysis is required. Continuous time-activity observations, with documentation, must be made for the length of the operation.

Correlating the possible measurement contributions from the documented activity based observations for the operation and for the surrounding area enables an effective means for understanding the primary contributors to nanoscale aerosols released from ENMs detected from the operation.

5.2.2 Near-Field Measurements: Comparative Measurements before and

The aerosol background level has to be determined, subject to operation specific circumstances,

- in the workplace before and after operations;

if this is impossible:

- outside the production plant,
- at a location, which is considered emission-free inside the production plant.

It is advisable to conduct continuous, long-term measurements over at least one hour to obtain information concerning the fluctuation of the aerosol background level. If extended continuous measurements are technically not feasible, short-term measurements may be conducted instead. However, it is advisable to conduct several short-term measurements to ensure sufficient reliability of the data [TRGS 402]. In the workplace the aerosol background level can either be determined at the location, where maximum nanoscale aerosols are expected to be released from ENMs (worst-case exposure situation) or as close to the worker as possible (pseudo-personal exposure situation).noscale aerosols released from ENMs detected from the operation.

It is preferable to conduct several measurements in defined intervals after operations to assess the decay curve of the aerosol concentration after a potential ENM release during operations.

It is recommended to conduct these measurements until the aerosol concentration has returned to the aerosol background level prior to the work commencing.

5.2.3 Far-Field Measurements: Simultaneous Measurements close to the Emission Source and at a Defined Reference Measurement Position

If the particle concentration is measured to determine the aerosol background concentration during the task at locations farther away from the possible emission source in the same or outside the work area, the farfield measurement approach is often preferred.

Specifically in buildings with natural ventilation it is useful to measure outside the building to determine the variation of the aerosol background concentration compared to the potential emission of nanoscale aerosols released from ENMs at the same time. In the case of mechanical ventilation, which may also include filtration of the exhaust air, it may be useful to choose a location near to the inlet of supply air into the building inside the premise as the reference measurement position. If this is not possible, the fluctuating aerosol background concentration may be measured in the same work area with sufficient distance to the potential emission source independently from the task.

5.3 Validation Procedure and Experiences from Validation

Regular calibration of measurement devices and the validation of results is essential. For the calibration it needs to be distinguished whether the device measures sizeresolved or size integrated. The validation of the sizing accuracy is easily done by dispersing spherical Polystyrene Latex (PSL) calibration particles. PSL particles can be bought off the shelf with specific and certified diameters and comparison of the measured size with the known particle size provides direct indication of the sizing accuracy of the device. Validation of the accuracy concerning concentration measures is not straight forward. Rather cumbersome number concentration calibration procedures have been suggested [Koch], [Fletcher]. A standard for number concentration calibrations is currently under development [ISO 3]. According to this standard particles with a narrow size distribution are produced with an electrospray, neutralized and then mobility-classified with a DMA to assure that every particles bears only a single elementary charge. Downstream of the DMA an electrometer measures the particle induced current. Due to the single charge on every particle the current can be easily transferred into the number concentration, which is used as the reference for the number concentration measurement device (e.g., CPC) which measures in parallel. This procedure requires extensive equipment and experience and is therefore rather intended as a calibration method for the device manufacturers but cannot be used for routine calibration check by end users. Instead it is usually preferred to compare the results of several simultaneous sampling devices of the same or similar type. This approach provides information on the comparability of devices, which is often more important than the exact accuracy of the measurement device, especially when several devices are employed in an or both size-resolving and size-integrating measurement devices. The most crucial requirement for such intercomparison studies is homogeneity of the test aerosol during each experimental run to assure that all devices sample identical aerosols concerning particle sizes and concentrations. Test aerosols should include a variety of sizes, morphologies and concentrations. Concentration ramps may also be applied to test the dynamic behaviour of the devices. In such intercomparison studies, one device should be treated as an internal reference. Results of all other devices are compared with this internal standard. The device which is expected to deliver the most reliable results, e.g., based on recent manufacturer calibration, should be chosen as internal reference.

An intensive comparison of mobility particle sizers was published recently [Asbach 1]. Cubic sodium chloride particles were used with 35 nm mode electrical mobility diameter and agglomerated diesel soot particles with 82 nm mode electrical mobility diameter. Both aerosols were sampled at different concentration levels. Furthermore, they were compared with different instrument settings to assess their influence. A calibrated SMPS was chosen as internal reference based on positive experience. The study revealed that all devices delivered very comparable results concerning particle sizing (usually within ± 5%), but deviations of ± 30% of the measured concentrations were not uncommon. One conclusion was that exact adjustment of flow rates of mobility particle sizers is essential.

6 Constraints of the Present Tiered Approach

6.1 Measurement Ranges and Limitations of the Equipment

For the time being industrial hygienists typically use total particle number concentration as the preferred metric to selectively assess nanoscale aerosols released from ENMs at the workplace (see chapter 3.2).

Widely-used instruments for detecting nano-objects have typically measurement ranges, which do not match the size range of the nanoscale as defined in ISO TS 27687:2008 (compare chapter 3.1). The measurement data collected in the workplace using these instruments may thus also include microscale primary objects, which are not aggregates or agglomerates of nano-objects. Furthermore, the methodologies usually deliver an equivalent diameter, but not the real physical dimensions of the nano-objects.

Examples of such methods are summarized in ISO TS 27628, annex A [ISO 1].

Tier 2 exposure measurement uses equipment, which will detect total particle number concentration according to the measurement ranges of the instrument. Condensation particle counters (CPC) are most commonly used for measuring this parameter. The equipment as currently available from different vendors has different measurement ranges (from a few nm up to the sub-µm range) and may also have different detection principles. The equipment will thus not necessarily deliver comparable data as the consequence, which will limit the opportunity for a metaanalysisand will also have an impact on the definition of a widely applicable interference value in tier 2.

Comparative measurements with 15 instruments with different detection principles have been recently conducted with various ENMs at different concentrations by a German group of experts in the field [Asbach 2].

Tier 3 exposure assessment requires additional instruments: An instrument to detectalso particle size distribution in the nm up to the µm range and in addition also sampling systems for subsequent off-line analysis.

Total particle number concentration and total particle size distribution from the nm range up to about 1 µm can be measured using Scanning Mobility Particle Sizers (e.g., SMPS). If the detection of larger objects is required, Optical Particle Counter (OPC) can be employed, which have a measurement range up to a few 10 µm and will cover the inhalable dust fraction.

Unfortunately, these instruments have the same limitations as the CPCs in Tier 2 exposure measurement. Furthermore, instruments of the same type but from different vendors may use different algorithms to process the raw data and therefore produce different results. Thus, the results could differ substantially depending on the device developer, measurement principle and correction algorithm, but also on the chemical composition of the aerosol and the shape of the nano-objects. A comparison of different instruments was conducted in the German project NanoCare, which was funded by the Federal Ministry of Education and Research (BMBF) [Asbach 1]. Identification of chemical identity requires sampling systems in addition.

- Sampling of primary nano-objects for off-line analysis with electron microscopy (SEM or TEM):
  Various sampling devices are available at the market utilizing different collection principles like electrostatic or thermal precipitators. The detection limits of these instruments are depending on various factors, for example on collection efficiency, flow rate, aerosol background level, size of the nano-objects and the analyzed filter area. In order to evaluate the results and unless a case-by-case evaluation was conducted to assess the absolute detection limit for single nanoobjects, the general limitations of the sampling devices have to be considered, Comparative measurements are conducted in the ongoing German project CarboSafe [Carbo Safe], which is also funded by the Federal Ministry of Education and Research.
- Sampling on filters for chemical analysis of the aero sol: If filters e. g. membrane filters of cellulose esters are employed, the detection limit is dependent on the filter efficiency, the background levels in the aerosol and in the filter material itself and on collection volume. As a universal approach established protocols to measure the respirable dust fraction could be used. However, the definition of the detection limit may also be assessed on a caseby-case basis.

6.2 Constraints of the Decision Logic

The limitation of the present decision logic is directly linked to the described deficiencies of the devices associated with the methodologies proposed by Tier 2 and Tier 3. For the decision logic relevant limitations are

- insufficient sensitivity of the gravimetric sampling me thodologies to assess the mass concentration,
- mismatch of the measurement range and the nanos cale (for some of the direct reading, counting devices),
- limited efficiency of sampling devices to collect representative filter samples for subsequent chemical or electron microscopic analysis.

6.2.1 Insufficient Sensitivity and Mismatch of the Measurement Ranges

The mass concentration is measured by gravimetric determination of filter samples according to established protocols (see chapter 4.6). As the mass of individual nano-objects and their nanoscale aggregates and agglomerates is only very small the assessment of the mass concentration of nanoscale workplace aerosols released from ENMs requires usually very long sampling times. In many cases, especially in case of batch processes, it may not be possible to measure the mass concentratioon at all due to insufficient sensitivity of the method. Furthermore, the gravimetric Due to the discussion of the appropriate metric, the total particle number concentration and in many cases the particle size distribution is also measured employing direct reading, counting devices, e.g., a CPC or a SMPS (see chapter 4.6 and 5). However, this equipment may have different sensitivity and does measure the aerodynamic or the mobility diameter of the airborne particulates as it is based on different measurement principles. Furthermore, the devices have different measurement ranges and some do not allow to selectively assess the nanoscale range. Thus, in some cases, e.g., if a CPC is employed, it may be not possible to separate the collected exposure data of the nanoscale from larger fractions. The practitioner will then be challenged to decide how to characterize the nanoscale aerosol background concentration and he also needs to decide if the interference value would be met or exceeded, if he refrains from applying higher tier equipment. Assessment will capture all airborne particulates in the workplace including the nanoscale fraction.

6.2.2 Representative Sampling

One constraint of this approach is that emissions including confounding release sources, such as soot emitted e.g., from diesel engines of trucks or fork lifts have to be excluded as far as possible. Evidence of the presence of a nanoscale aerosol released from ENMs in the workplace can thus be obtained only with reasonable certainty, if the chemical identity of the airborne particulates is determined. This also requires the collection of representative filter samples and thus the use of suitable sampling devices. However, depending on the sampling principle [Fierz], [Fissan], [Sundermann], [Wen], the sampling efficiency is usually low to moderate only. The practitioner will thus have to be cautious to draw robust conclusions from a negative result.

7 Conclusions and Outlook

The presented tiered approach was developed in a dialogue by the Institute of Energy and Environmental Technology e.V. (IUTA), the Federal Institute for Occupational Safety and Health (BAuA), the German Social Accident Insurance Institution for the Raw Materials and Chemical Industry (BG RCI), the Institute for Occupational Safety and Health of the DGUV (IFA), the Technical University Dresden (TUD) and the German Chemical Industry Association (VCI). It represents a pragmatic approach to an exposure assessment of nanoscale aerosols released from engineered nanomaterials in the workplace. The approach combines established risk management concepts with elements of exposure assessment according to the current technology, and it is based on the experience of the participating practitioners. The institutions involved in the current dialogue came to the following conclusions:

- A pragmatic exposure measurement strategy of nanoscale aerosols released from ENMs is a crucial element of the risk assessment and thus is essential for the safety and health of occupational workers.
- Such a strategy would meet all legal requirements for workplace safety. Existing legally binding OELs, e.g. synthetic amorphous silica [TRGS 900: EC No. 231-545-4], carbon black [ACGIH], etc., have to be complied with.
- As further legal requirements evolve and, e.g., new definitions of nanomaterials for regulatory purposes are being developed, the challenges of the implemen tation of such requirements in practice have to be discussed further, both within the industrial hygiene community itself as well as with national authorities.
- The consequences of the current discussion on a de finition of ENMs for regulatory purposes must be more deeply considered in the context of state-of-the-art industrial hygiene practice as such definition determines not only the boundaries of the workplaces affected but also the equipment of choice and thus the measurement methods.
- If regulation is to result in an effective and efficient legal framework for the benefit of a high level of work place safety, the challenges for practitioners imposed by the limitations of available measurement devices and shortfalls of measurement methods must also be taken into account.
- The proposed decision logic for the assessment of measurement data, which is based on three criteria, is novel. This pragmatic concept leads to different cases, which may guide the decision of the practitioner how to best proceed in the assessment of risk in the workplace.
- In view of the limitations of the currently available measurement equipment, which define the boundaries of this step-by-step approach, further equipment development is required to better suit the demands in practice (keywords: sensitivity, accuracy, measurement range and representative sampling).
- Despite the current uncertainty of the relevant measurement parameter (keywords: mass vs. total particle number or surface area concentration), the approach proposed by this document may yet be considered as a best practice, which may be revisited as soon as new scientific findings especially as binding, health-based occupational exposure limit values become available.
- And finally, the presented approach may serve as a starting point for further international harmonization of exposure assessment to nanoscale aerosols released from engineered nanomaterials and thus will contribute to improved industrial hygiene at nanotechnology workplaces and comparable data quality for later use and review.

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Annex 1: List of Abbreviations

ACC	American Chemical Council
ACGIH	American Conference of Governmental and Industrial Hygienists
AD	Aerodynamic Diameter
AES	Atomic Emission Spectroscopy
BAuA	Federal Institute for Occupational Safety and Health
BG RCI	German Social Accident Insurance Institution for the Raw Materials and Chemical Industry
BMBF	Federal Ministry of Education and Research
BOELV	Binding Occupational Exposure Level Values
BSI	British Standards Institute
CARACAL	Competent Authorities for REACH and CLP
CASG	Nano Competent Authority Subgroup Nano
CPC	Condensation Particle Counter
CMR (compounds)	Cancerogenic, Mutagenic, Reproductive Toxic (compounds)
CNT	Carbon Nanotube
DEHS	Di-Ethyl-Hexyl-Sebacat
DMA	Differential Mobility Analyzer
ELPI	Electrical Low Pressure Impactor
ENM	Engineered Nanomaterial
HEPA (filter)	High-Efficiency Particulate Air (filter)
IFA	Institute for Occupational Safety and Health of the DGUV
IUTA	Institute of Energy and Environmental Technology e.V.
IOELV	Indicative Occupational Exposure Level Values
JRC	Joint Research Center
LOQ	level of qunatification
µm	micrometer
MSDS	Material Safety Data Sheet
MWCNT	Multi-Walled Carbon Nanotubes
nm	nanometer
NSAM	Nanoparticle Surface Area Monitor
OECD	Organization for Economic Cooperation and Development
OEL	Occupational Exposure Level
OPC	Optical Particle Counter
PEROSH	Partnership for European Research on Occupational Safety and Health
PSL	polystyrene latex
SCENIHR	Scientific Committee on Newly Identified Health Risks
SEM	Scanning Electron Microscopy
SME	Small and medium enterprises
SMPS	Scanning Mobility Particle Sizer
SOP	Standard Operating Procedure
TEM	Transmission Electron Microscopy
TNO	Netherlands Organization for Applied Scientific Research
TUD	Technical University Dresden
VCI	German Chemical Industry Association

Annex 2: Substances Listed in the OECD Testing Program

- fullerenes (C60)
- single-walled CNTs
- multi-walled CNTs
- silver nanoparticles
- gold nanoparticles
- iron nanoparticles
- titanium dioxide
- aluminium oxide
- cerium oxide
- zinc oxide
- silicon dioxide
- dendrimers
- nanoclays

Annex 3: Literature

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