The EU FP7 NanoDefine Project

Development of an integrated approach based on validated and standardized methods to support the implementation of the EC recommendation for a definition of nanomaterial

Catalogue of technical methods performance criteria for nanomaterial characterisation

NanoDefine Technical Report D7.1

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The NanoDefine Consortium 2013

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NanoDefine in a nutshell

The EU FP7 NanoDefine project was launched in November 2013 and will run until October 2017. The project is dedicated to support the implementation of the EU Recommendation on the Definition of Nanomaterial by the provision of the required analytical tools and respective guidance. Main goal is to develop a novel tiered approach consisting of (i) rapid and cost-efficient screening methods and (ii) confirmatory measurement methods. The "NanoDefiner" eTool will guide potential end-users, such as concerned industries and regulatory bodies as well as enforcement and contract laboratories, to reliably classify if a material is nano or not. To achieve this objective, a comprehensive inter-laboratory evaluation of the performance of current characterisation techniques, instruments and software is performed. Instruments, software and methods are further developed. Their capacity to reliably measure the size of particulates in the size range 1-100 nm and above (according to the EU definition) is validated. Technical reports on project results are published to reach out to relevant stakeholders, such as policy makers, regulators, industries and the wider scientific community, to present and discuss our goals and results, to ensure a continuous exchange of views, needs and experiences obtained from different fields of expertise and application, and to finally integrate the resulting feedback into our ongoing work on the size-related classification of nanomaterials.

Bibliographic data

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1 Abbreviations and acronyms

CM	Characterisation Methods
CNT	Carbon nanotube
CRM	Certified Reference Material
DLS	Dynamic Light Scattering
e-beam	Electron beam
EC	European Commission
EM	Electron Microscopy
MFM	Magnetic Force Microscopy
SEM	Scanning Electron Microscopy
UV-Vis	Ultraviolet-Visible

2 Summary

In this technical report, a catalogue of technical performance criteria targeted at measurement requirements for the purpose of this project is detailed. Other criteria, beyond those addressing the purely technical performance, such as the required economical effort, are not included here in this NanoDefine Technical Report D7.1. However, those criteria are important for the decision process and consequently they will be considered and included in the NanoDefine Technical Report D7.4 (Set of criteria with ranking system to steer the decision process) and the NanoDefiner decision support framework.

Objectives of this NanoDefine Technical Report D7.1 are detailed in part 3 (Introduction). Technical performance criteria according to the substance to analyse are described in part 4 (Applicability to different groups of substances) following key and optional parameters such as substance nature, particle shape, thermal degradation and e-beam sensitivity. Moreover, method-inherent criteria are reported in part 5 (Method performance parameters and criteria). To conclude, a table which summarizes all the criteria depending on the substances to analyse and depending on the characterisation method itself is provided.

3 Introduction

The task of the NanoDefine Technical Report D7.1 consists in developing a catalogue of technical performance criteria targeted at measurement requirements resulting from the EC definition of nanomaterial.

One of the WP7 objectives is to establish the NanoDefine e-tool for methods selection, data evaluation and size-related classification of particulate materials according to the definition. This tool, with options based on material type, purpose, required data quality (including confidence level), will guide the user to the most reliable measurement method to identify/classify any substance or mixture according to the definition. The user will be provided with precise guidance which will allow extending the measurement to the widest possible range of substances, mixtures, and encompass also products and (other) matrices. To this aim, a catalogue of technical performance criteria is proposed here to evaluate characterisation methods. This catalogue and the material classification system will be the entry points for the NanoDefiner decision support flow-scheme .

Performance criteria of each measurement method have to be elaborated in detail and include:

- Applicability to different groups of substances (chemical scope of the method)
- Applicability to polydisperse samples
- Measurement in terms of size and in terms of test medium for different groups of substances
- Capacity to measure aggregates, agglomerates, primary particles and/or non - spherical particles.
- Accuracy of the results determined with the CM
- Standardization status (traceability of the measured values / availability of CRMs)

All potentially suitable characterisation methods will be quantitatively evaluated against these criteria in other technical reports, and ranked against each other.

The aim of NanoDefine Technical Report D7.1 is also to develop a general performance requirement document for methods to be included in the decision support framework, taking also in account the decision criteria developed in NanoDefine Technical Report D7.3 and D7.4. These performance requirements will be applicable also to future methods to decide in the decision support framework i.e., whether they can be used to test materials according to the EU requirements and its subsequent amendments, including also its sector specific implementations. The general performance requirements document will support the EU Commission in developing formal decision criteria when implementing the EU definition. It will guarantee the sustainability and flexibility of the decision support framework after the end of the project, as technologies advances.

The characterisation performance criteria have to be evaluated against criteria de-pending on the sub-stance to analyse (if the characterisation method is suitable for this type of substance) and depending on the technical factors. The order of the crite-ria is not listed according to their priority in this document.

4 Applicability to different groups of substances

4.1 Nanoparticles in powder, or liquid suspensions or embedded in a matrix

Certain characterisation methods are only suitable or more suitable for nanoparticles dispersed in a liquid phase, others for aerosols or for solid state powders and granulates. It is also useful to know if a method can characterise nanoparticles when they are embedded in a matrix (this includes final products). Some nanoparticles change significantly during sample preparation, thus excluding certain techniques. Therefore the primary grouping is done by the sample physical state:

- Dispersed in liquids (pure or not)
- Solid particulate form (powder...)
- Dispersed or embedded in different kinds of matrices (paste, resin, elastomer...)

4.2 Dispersibility according to dispersion protocols

Some characterisation methods only work on dispersions (liquid and gas). It is essential to know if the substance to analyse can be dispersed by standardized protocols that specify both a dispersion medium and a dispersion protocol. Size distribution can be affected by the sample preparation protocol, such as the choice of the dispersion media and the particle concentration and also by aggregation and agglomeration if the liquid is not appropriate.

The presence of surface properties which includes functionalisation can be decisive to which group the material belongs.

- Dispersible in aqueous media (by generalized protocols)
- Dispersible in non-polar liquids (by generalized protocols)
- Dispersible in polar liquids (by generalized protocols)
- Dispersible in material-specific media and protocols
- Can be aerosolized

4.3 Substance Nature

One of the most important criteria is the nature of the substance since the characterisation method has to be chosen and/or adapted accordingly. For example, a UV-Vis spectrometer can only serve as size measurement method if the material exhibits Surface Plasmon Resonances, e.g. silver or gold nanoparticles.[1]

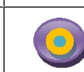
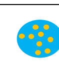
- Inorganic materials such as metals, ceramics, salts, oxides (significant content of inorganic elements homogeneously incorporated in all constituent particles)

  - Particles which exhibit size-dependent absorption of photons / fluorescence (metals, quantum dots[2]…)
- Carbon-based (CNT, Nanodiamond, Carbon Black…)
- Organic, particular (Polymers, dyes, etc., nanonized, precipitated)
- Organic, non-particular (Dendrimers, Liposomes, Supramolecular assemblies…)
- Biological (nucleic acid, peptide, protein)
- Composite
- Other

4.3.1 Composite structure

If the substance is a composite material (composed of different types of material) it can be important to know more about its structure in order to apply a suitable characterisation method including the correct data evaluation. Under certain circumstances, some characterisation methods can distinguish between core/shell nanoparticles and nanoparticles with multiple coatings. For example, in the case of nanoparticles with a gold core and a silica shell, both the silica shell thickness and the core size could be evaluated by UV-Vis measurement under certain circumstances.[3] If the shell is organic, Dynamic Light Scattering (DLS) and Electron Microscopy (EM) will give different results because DLS measures hydrodynamic radius. Materials with such a composite structure may be classified as suggested below:

- Core/shell
- Multiple coating
- A mix of two or more different materials

Core-shell nanoparticles are nanoparticles which have a core of one material embedded in another material type.	
Nanoparticles with multiple coatings are covered by successive layers of various materials.	
Nanoparticles composed by a mix of two or more different materials are made from a combination (homogenously or not) of different kinds of materials.	

The structure of a composite material is important because it can lead to different results according to the characterisation methods employed. Hence, it is necessary to know if a specific technique is able to determine the particle size without interference caused by the composite structure

4.4 Particle shape and number of dimensions in the nanoscale

Some methods may be unsuitable for certain particle shapes. In this context, it is also important to know how many dimensions are in the nanoscale.

The number of nanoscale dimensions can be:

- 1
- 2
- 3

The shape of nanomaterials can be classified as below:

- Sphere
- Equiaxial (Prismatic, Cubic, Tetrahedral)
- Elongated (Tubes, fibres, rods)
- Flat (Flakes and discs)
- Other

4.5 Thermal degradation sensitivity

Some of characterisation methods may lead to a thermal load on the sample. Due to their structure or their nature, some substances may change upon such thermal treatments. It is important to know if characterisation methods can cause damages to heat sensitive samples, which would destroy the validity of the measurements. Nano-particles may be classified as below:

- Sensitive above 0 °C
- Sensitive above 25 °C (room temperature)
- Sensitive above 37 °C (body temperature)
- Sensitive above 50 °C
- Sensitive above 100 °C
- Sensitive above 150°C
- Sensitive above 500 °C
- Sensitive above 1000°C

4.6 Cooling degradation sensitivity

It is important to know if characterisation methods can cause damages during cooling of sensitive samples, which would destroy the validity of the measurements.

- Sensitive below 25 °C
- Sensitive below 0 °C
- Sensitive below - 18 °C (freezer)
- Sensitive below - 35 °C (deep freezer)
- Sensitive below - 78 °C (dry ice)
- Sensitive below - 195°C (liquid nitrogen)

4.7 E-beam sensitivity

Some substances are sensitive to e-beam, and cannot be characterised reliably with EM, or require more sophisticated EM techniques, such as cryo-EM or low-dose techniques. This criterion enables to know if it would be relevant to analyse those substances with the respective method.

- Sensitive to e-beam
- Not sensitive to e-beam

4.8 Sample dispersity and modality

Almost all samples are polydisperse to a certain degree. Therefore it is important to know if the characterisation methods can analyse a polydisperse sample without providing false results. This factor has to be considered in the performance of the methods.

- Monodisperse sample
- Polydisperse sample
- Multimodal sample
- Monomodal sample

It is also important to define at which degree of polydispersity a sample may not be considered monodisperse anymore.

4.9 Optional criteria

4.9.1 Electrical conductivity

Some characterisation methods are more suitable for electrically conductive substances.

- Conductive
- Semiconductive
- Insulator

4.9.2 Magnetic properties

Magnetic particles may be measured with some specific characterisation methods such as magnetic force microscopy (MFM)[4] or magnetic particle spectrometer.[5,6] Thermomagnetic,[7] dc magnetization[8] and ac susceptibility[8] measurements enable also to determine the size distribution of magnetic particles. In this regard, nanoparticles could be classified as:

- Magnetic
- Non magnetic

4.9.3 Functionalization / no functionalisation

One important criterion is to know if the nanoparticles are functionalised or not. Characterisation methods have to be adapted according to this feature. More details about functionalisation will be given in the NanoDefine Technical Report D7.3 (material classification system).

- Functionalised
- Not functionalised

It would be also important to determine the difference between functionalisation and shell layer. If nanoparticles are completely covered with a uniform layer, nanoparticles would belong to the composite category.

4.9.4 Agglomeration/ aggregation state

Some substances are aggregated or have a tendency to agglomerate, something which needs to be accounted for in the data analysis. From this point of view, the nanoparticles can be classified as:

- Nanoparticles are aggregated
- Nanoparticles are not aggregated
- Nanoparticles are agglomerated
- Nanoparticles are not agglomerated

5 Method performance parameters and criteria

5.1 Counting, separative or ensemble techniques

- Single particle counting
- Calculate number or concentration from ensemble methods
- Method combination (hyphenated methods)

5.2 Working range

Range in which the method provides reliable results (may be dependent also on the material and its preparation and on instrument type). Units need to be given.

- Size range
- Concentration range
- Minimum sample intake (How much material is needed?)
- Linearity/proportionality
- Limits of detection/quantification
- Sensitivity (Counting or detection efficiency as a function of size)

5.3 Trueness

Difference between the average of several measurements on the same sample or material and the true value of the measured property (associated quantitative term "bias").

This is either in terms of size or in terms of amount of particles.

Trueness in weighting the size fractions has to be specified. (Ratio between measured and true amount of a certain size fraction)

5.4 Robustness

Influence of slight variations in the test protocol on the outcome of the test.

5.5 Precision

Test result variation within one test series (repeatability) or several test series (intermediate precision), either in terms of size or in terms of amount of particles.

5.6 Resolution

To which degree a certain size fraction can be distinguished from another (e.g. minimum distance or size ratio needed between different modes so that they can be identified in a mixture of monodisperse samples).

5.7 Size distribution

Does the method provide a size distribution[10] or a certain average value?

5.8 Selectivity

How well can nanoparticles according to the EC definition be discriminated from

- non-nanoparticles of the same composition
- non-nanoparticles of another composition (matrix particles)
- nanoparticles of another composition

Moreover, if the substance to analyse is not pure, it is essential to know if and how the results are affected by impurities, including dissolved ionic species from the same substance.

5.9 Capability to measure aggregation

Can the method identify and/or measure agglomerates or aggregates of particles?

5.10 Capability to measure single particles

Can the method measure the size and number of individual particles?

5.11 Counting constituent particles in aggregates

Is the method is able to count constituent particles in aggregates?

5.12 Composition

Does the method provide information on the chemical composition?

5.13 Specification of the measurand (diameter)

Size measurement is method dependent. [11] Different methods address different measurands (equivalent diameters) which need to be specified (hydrodynamic diameter, Stokes diameter, projected area diameter, etc.).

5.14 Non-destructive / destructive

This is to indicate whether the method is destructive or not.

6 Conclusions

Characterization methods can be ranked with this table. In the first part (blue rows), related to the substance to analyse, it is necessary to evaluate if the methods are suitable for these types of materials or not (yes/no). In the second part (yellow rows), related to the technique, it is necessary to specify the characteristics of each characterisation method according to the criteria.

Table 1: Summary of technical performance criteria

Criteria	Criteria	Characterization
Nanoparticles in powder or liquid suspensions or embedded in a matrix	Dispersed in liquids	
	Solid particulate form	
	Dispersed or embedded in different kinds of matrices	
Dispersibility by dispersion protocols	Dispersible in aqueous media	
	Dispersible in non-polar liquids	
	Dispersible in polar liquids	
	Dispersible in material-specific media	
	Can be aerosolized	
Substance Nature	Inorganic	
	Size-dependent absorption / fluorescence	
	Carbon based	
	Organic, particulate	
	Organic, non-particulate	
	Biological	
	Composite	
	Other	
Composite	Core/shell	

	Multiple coatings	
	A mix of two or more different materials	
Number of nanoscaled dimensions	1	
	2	
	3	
Shape of nanoparticles	Sphere or assimilated	
	Equiaxial	
	Tubes, fibres, rods	
	Flakes and discs	
	Other	
Thermal degradation sensitivity	Above 0°C	
	Sensitivity above 25°C	
	Sensitivity above 37°C	
	Sensitivity above 50°C	
	Sensitivity above 100°C	
	Sensitivity above 150°C	
	Sensitivity above 500°C	
	Sensitivity above 1000°C	
Cooling degradation sensitivity	Sensitive below 25 °C	
	Sensitive below 0 °C	
	Sensitive below -18 °C	
	Sensitive below -35 °C	
	Sensitive below -78 °C	
	Sensitive below -195 °C	
E- beam sensitivity	e- beam sensitive	
	Not e-beam sensitive	
Sample dispersity and modality	Monodisperse sample	
	Polydisperse sample	
	Monomodal sample	

	Multimodal sample	
Conductivity properties	Conductive	
	Semiconductive	
	Insulator	
Magnetic properties	Magnetic	
	Non magnetic	
Functionalization / no functionalisation	Functionalised	
	Not functionalised	
Agglomeration/ aggregation state	Nanoparticles are aggregated	
	Nanoparticles are not aggregated	
	Nanoparticles are agglomerated	
	Nanoparticles are not agglomerated	
counting, separative or ensemble techniques	Single particle counting	
	Calculate number or concentration from ensemble methods	
	Method combination (hyphenated methods)	
Working range	Size range	
	Concentration range	
	Minimum needed sample	
	Linearity/proportionality	
	Limits of detection/quantification	
	Sensitivity (Counting efficiency) as a function of size	
Limits of detection/quantification	What is the lower limit to detect	
Trueness	Indicate the trueness of this CM	

Trueness in weighting the size fractions	Specify the trueness in weighting the size fractions of this CM	
Robustness	Specify the robustness of this CM.	
Precision	Specify the precision of the CM	
Resolution	Specify the resolution of this CM	
Size distribution	Is it possible to measure size distribution?	
Selectivity	discrimination from non-nanoparticles of the same composition	
	discrimination from non-nanoparticles of another composition (matrix particles)	
	discrimination from nanoparticles of another composition	
	Impurities	
Measures aggregation	Is it possible to measure aggregation or agglomeration of particles?	
Measures individual particles	Does this CM measure individual particles?	
Counting constituent particles in aggregations	Is the method able to count constituent particles in aggregates?	
Composition	Does this CM analyse composition?	
Specification of the type of size (diameter)	Specify: for example hydrodynamic…	
Destructive method or not	Is it a destructive method?	

Other Specificity		

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