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An overview of concepts and terms
used in the European Commission's
definition of nanomaterial

H. Rauscher, G. Roebben, A. Mech, N. Gibson,
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Front page image: graphic elaboration of Figure 2.2, plate-like shapes: Au “nanocoins” on polymer substrate (SEM image by A. Valsesia, Joint Research Centre, © European Commission)

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An overview of concepts and terms used in the European Commission's definition of nanomaterial

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Executive Summary

The European Commission's Recommendation on a definition of the term 'nanomaterial'^a (EC NM definition) provides a general basis for regulatory instruments across all areas of European Union policy, and a common understanding of its concepts and terms is necessary for its implementation. The definition, or core parts of it, has been utilised in sector specific EU legislation, (e.g. Biocidal Products Regulation, Medical Devices Regulation, annexes of REACH) and is also used in several EU national schemes.

This report aims to provide clarifications of the key concepts and terms that are used in the EC NM definition, and discusses them in a regulatory context. Corresponding to the broad scope of the definition, the considerations in this report can be applied across all relevant legislative areas; they are not specific to any particular piece of legislation. The report therefore supports a harmonised and coherent implementation of the EC NM definition in any specific regulatory context at Community and national level.

The EC NM definition may apply to any particulate material, regardless of whether it is natural, incidental or man-made, and it is based on the only feature that is common to all nanomaterials: nano-scale external particle dimensions (particles being minute pieces of matter with defined physical boundaries). The definition covers only particulate materials that are solid at normal temperature and pressure (NTP), i.e. 298.15 K and 101,325 Pa. External particle dimensions can be represented in various ways, e.g. by the minimum Feret diameter and/or the maximum inscribed circle diameter.

The EC NM definition does not cover nanostructured materials (materials with nanoscale internal or surface structures) unless the external particle size criteria are met. Single molecules are not considered as particles, with the exception of fullerenes, graphene and single-wall carbon nanotubes, which are explicitly included by derogation.

It should be emphasised, that a definition based only on size properties cannot differentiate between hazardous and non-hazardous materials. The term *material* is generic and independent from specific legislation. Within a specific regulatory context it may be replaced by what is covered and regulated by that sector specific legislation, e.g. substance, ingredient, etc.

^a European Commission, 'Commission recommendation of 18 October 2011 on the definition of nanomaterial' (2011/696/EU), Off. J. Eur. Union L275, p38–40, 2011.

Constituent particles are the morphologically identifiable particles inside an aggregate or agglomerate. For the implementation of the EC NM definition it is not necessary to distinguish between aggregates and agglomerates. Mobility-based techniques cannot be used to measure the size of constituent particles in aggregates and agglomerates.

If 50 % or more of the constituent particles of a material in the number size distribution have one or more external dimensions in the size range 1 nm to 100 nm, then the material is a nanomaterial. It should be noted that a fraction of 50 % with one or more external dimensions between 1 nm and 100 nm in a number size distribution is always less than 50 % in any other commonly-used size distribution metric, such as surface area, volume, mass or scattered light intensity. In fact it can be a tiny fraction of the total mass of the material.

Even if a product contains nanomaterials, or when it releases nanomaterials during use or ageing, the product itself is not a nanomaterial, unless it is a particulate material itself that meets the criteria of particle size and fraction.

The volume specific surface area (VSSA) can be used under specific conditions to indicate that a material is a nanomaterial. VSSA is equal to the sum of the surface areas of all particles divided by the sum of the volumes of all particles. $VSSA > 60 \text{ m}^2/\text{cm}^3$ is likely to be a reliable indicator that a material is a nanomaterial unless the particles are porous or have rough surfaces, but many nanomaterials (according to the principal size-based criterion) will have a VSSA of less than $60 \text{ m}^2/\text{cm}^3$. The $VSSA > 60 \text{ m}^2/\text{cm}^3$ criterion can therefore only be used to show that a material is a nanomaterial, *not vice versa*. The VSSA of a sample can be calculated if the particle size distribution and the particle shape(s) are known in detail. The reverse (calculating the size distribution from the VSSA value) is unfeasible.

Finally, suitable sample preparation, appropriate measurement methods, a robust reference system and an integrated decision flow scheme are key elements for a reliable identification of nanomaterials.

1 Introduction

In 2011, the European Commission (EC) adopted the following Recommendation (2011/696/EU) for a definition of the term nanomaterial [1], in the following called the 'EC NM definition' in this report:

'Nanomaterial' means a natural, incidental or manufactured material containing particles, in an unbound state or as an aggregate or as an agglomerate and where, for 50 % or more of the particles in the number size distribution, one or more external dimensions is in the size range 1 nm-100 nm.

In specific cases and where warranted by concerns for the environment, health, safety or competitiveness the number size distribution threshold of 50 % may be replaced by a threshold between 1 and 50 %.

The EC NM definition further specifies:

By derogation [...], fullerenes, graphene flakes and single wall carbon nanotubes with one or more external dimensions below 1 nm should be considered as nanomaterials.

[...] 'particle', 'agglomerate' and 'aggregate' are defined as follows:

(a) 'particle' means a minute piece of matter with defined physical boundaries;

(b) 'agglomerate' means a collection of weakly bound particles or aggregates where the resulting external surface area is similar to the sum of the surface areas of the individual components;

(c) 'aggregate' means a particle comprising of strongly bound or fused particles.

Where technically feasible and requested in specific legislation, compliance with the definition [...] may be determined on the basis of the specific surface area by volume. A material should be considered as falling under the definition [...] where the specific surface area by volume of the material is greater than 60 m²/cm³. However, a material which, based on its number size distribution, is a nanomaterial should be considered as complying with the definition [...] even if the material has a specific surface area lower than 60 m²/cm³.

The EC NM definition was developed to provide a common basis for regulatory purposes across all areas of European Union (EU) policy. Since its publication, regulatory provisions were adopted in the EU jurisdiction which explicitly address nanomaterials and contain regulatory definitions of the term 'nanomaterial'. The latter were derived from the EC NM definition, adopting it either as a whole or in its core parts, for example in:

- the Biocidal Products Regulation (EU) No 528/2012 [2];
- the Medical Devices Regulation (EU) 2017/745 [3];
- the annexes of the Chemicals Regulation REACH (EC) No 1907/2006, which were amended in 2018^b.

^b Commission Regulation EU 2018/1881 of 3 December 2018 amending Regulation (EC) No 1907/2006.

Furthermore, the EC NM definition, or core parts of it, is used already in some Member States (e.g. in France, Denmark, Sweden, Belgium) and in Norway to define a nanomaterial or (in France) a substance at the nanoscale for the purposes of national registration and notification schemes. The EC NM definition is also referred to in the EFSA Guidance on risk assessment of the application of nanoscience and nanotechnologies in the food and feed chain [4]. EFSA's Scientific Committee advises to take it (and any future reviews) into consideration when assessing the safety of materials consisting of particles.

It is therefore appropriate to support the implementation of the EC NM definition by (i) clarification of its key concepts and terms and (ii) practical guidance on how to identify nanomaterials through measurements, as this was voiced by numerous stakeholders in their responses to a survey carried out by the European Commission's Joint Research Centre (JRC) [5,6].

This report focusses on key concepts and general and specific terms and explains them in the context of the EC NM definition. A second report dedicated to measurements is currently in preparation and will give specific advice on how to identify materials based on the criteria laid down in the EC NM definition, mainly through analytical approaches.

These two reports are intended to facilitate the implementation of the EC NM definition in practice across all relevant legislative areas. The considerations are not specific to any particular piece of legislation and aim towards a harmonised and coherent implementation of the EC NM definition in any specific regulatory context at Community and national levels. Such horizontal considerations may be complemented later by additional sectoral guidance documents, e.g. targeted advice for groups of materials relevant for sector-specific legislation.

2 Key concepts and terms

2.1 Basic principles of the EC NM definition

The EC NM definition aims to be broadly applicable in EU and national legislation. It is a recommendation and hence not legally binding, but at the same time it aims at harmonising existing and future legislation with regard to using the term nanomaterial in a regulatory context.

The scope of the EC NM definition is in line with the European Parliament (EP) Resolution of 24 April 2009 on regulatory aspects of nanomaterials [7] calling for the introduction of a comprehensive science-based definition of nanomaterials, and that such a definition should be broadly applicable in EU legislation. The EC NM definition is generally in line with other approaches worldwide to identify nanomaterials. At the same time, it is more specific and quantitative than most other (often non-regulatory) definitions. For example, the International Organization for Standardization (ISO) defines the term 'nanoscale' as the length range approximately from 1 nm to 100 nm [8]. By using 'approximately' this definition explicitly avoids imposing well-defined size limits, which would be necessary for an unambiguous implementation in a legislative framework.

The EC NM definition only applies to materials containing (or consisting of) particles. As there are no generic relationships, valid for all materials, between particle size and physicochemical properties, the only feature that is common to all nanomaterials is their nano-scale physical dimensions. Hence, the EC NM definition is based on particle size and it categorises a material as nanomaterial if 50% or more of its constituent particles

fall in the size range from 1 nm to 100 nm, according to the particle number-based particle size distribution (or, for short, the number size distribution). This precise criterion enables its regulatory implementation.

Nanomaterials are not necessarily hazardous [9], therefore the EC NM definition is not based on hazard or risk assessment. It cannot differentiate between hazardous and non-hazardous materials as neither particle size nor specific surface area can be directly linked to hazard. It simply identifies, according to well-defined criteria, a certain group of materials as 'nanomaterial', which might deserve specific considerations in a regulatory context.

Identification of a material as a nanomaterial according to the EC NM definition is not determined by a certain (chemical) composition, a certain structure, novel properties that are attributable to the particles' external dimensions, or by the application of the material in a specific field. Exceptions are fullerenes, graphene flakes and single wall carbon nanotubes with one or more external dimensions below 1 nm, which are explicitly considered as nanomaterials.

Basic principles of the EC NM definition

- The EC NM definition is generally in line with other approaches worldwide, but it is more specific and quantitative than most other definitions. This enables its implementation in a regulatory framework.
- Nanomaterials are not necessarily hazardous and a definition based only on size properties cannot differentiate between hazardous and non-hazardous materials.
- The EC NM definition is based on the only feature that is common to all nanomaterials: their nano-scale physical dimensions. It categorises a material by the fraction of its constituent particles in a defined size range, measured on the basis of the particle number-based particle size distribution.

2.2 Origin of the material (natural, manufactured, incidental)

The EC NM definition refers to *natural, incidental and manufactured materials*. It therefore covers a potentially very large number of materials, regardless of whether these are new and man-made for a specific purpose, unintentional by-products of human activity, or whether they naturally occur in the environment.

Properties of and possible risks posed by a nanomaterial do not depend on whether an object is natural, produced incidentally, or is the result of an engineering process with or without the explicit intention to manufacture a nanomaterial. In that respect, natural materials can exhibit the same properties as those that are manufactured and *vice versa*. Therefore, it would not be coherent for a comprehensive nanomaterial definition to exclude certain types of materials just because of their origin. A definition with a narrow scope would not be useful for broad regulatory use if restrictions based on their origin were to be included.

The EC NM definition should not pre-judge nor reflect the scope of application of any piece of EU legislation or of any provisions potentially establishing additional requirements for those nanomaterials. In fact, certain sectoral legislation has tailored a nanomaterial definition to cover specific needs. Some of them address only 'engineered' (Novel Foods Regulation 2015/2283) [10] or 'intentionally produced' nanomaterials (Cosmetic Products Regulation 1223/2009) [11], while others include also 'natural' nanomaterials (Biocidal Products Regulation 528/2012) [2]. This may generate the need to distinguish between manufactured, incidental and natural nanomaterials in some sector-specific legislation. Nonetheless, for the generic application of the EC NM definition, such a distinction is not necessary as it addresses all materials regardless of their origin.

Origin of the material

- The EC NM definition applies to all materials regardless of their origin.

2.3 Nanomaterials vs. nanostructured materials

The EC NM definition is explicitly limited to materials containing (or consisting of) particles (i.e. particulate materials) and its provisions are designed to specifically address this type of material. This approach was inspired by earlier reports from SCENIHR [12] and the JRC [13], which stated that human and environmental exposure to particulate materials with a nano-specific character is more likely than exposure to materials with 'embedded' nanostructural features, or particles embedded in a solid matrix. Hence for a definition that denotes a class of materials that may require specific regulatory attention in legislation, particulate materials are most relevant.^c

The consequence of this focus on particulate materials is that materials defined as nanomaterials by other organisations or standardisation bodies may not necessarily be covered by the EC NM definition. For example, ISO includes in its definition of nanomaterial also materials with larger external dimensions (i.e. > 100 nm), if they have internal structures or surface structures in the nanoscale. On the other hand, certain types of nanostructured materials (according to the ISO definition) also fall under the EC NM definition as nanostructured materials can fulfil the EC NM definition.

Such materials are (i) nanostructured materials consisting of aggregates and/or agglomerates of particles, where at least half of those constituent particles have an external dimension between 1 nm and 100 nm. (ii) Particles with an internal or surface structure in the nanoscale but also with at least one external dimension between 1 nm and 100 nm. It should also be noted that if an external dimension(s) of a particle is in the nanoscale [8], ISO recommends the term nano-object.

The inclusion of other types of nanostructured materials not covered by the EC NM definition (e.g. materials consisting of particles with all external dimensions larger than 100 nm but with nanoscale surface structures, nanocomposite materials, nanoporous materials) would significantly change the scope of the EC NM definition. The broad scope of the term 'nanostructured' covers a large number of traditional materials. It should however be pointed out that specific legislation may always be developed if it becomes necessary to address (specific) non-particulate or nanostructured materials in certain regulatory fields.

Internal and surface structures

- Internal structures or surface structures in the nanoscale (nanostructured materials as per ISO) are of no relevance for the EC NM definition. Such materials are only considered nanomaterials if their external dimensions fulfil the EC NM definition.
- Agglomerates and aggregates are nanostructured materials, but they are implicitly covered by the EC NM definition, if at least half of their constituent particles have external dimensions between 1 nm and 100 nm.

2.4 The term ‘particle’

The EC NM definition limits the scope of the term nanomaterial to materials containing (or consisting of) particles, i.e. particulate materials. It is therefore important to have a common understanding of what is considered as a particle. The EC NM definition therefore follows the relevant ISO standard [14] and defines the term particle as *‘a minute piece of matter with defined physical boundaries’*.

The term ‘minute’ in the ISO definition indicates the relatively limited size of a particle. The vague designation ‘minute’ may be deliberately chosen, because ‘particle’ is used in different scientific and industrial fields which deal with particles of very different size. There are no official rules for when an item is considered ‘minute’, but when a material is to be assessed against the EC NM definition, it is often sufficient to analyse the particles with two or three orthogonal dimensions up to 100 micrometres. The materials can then be identified according to the outcome of that analysis, because usually there are much fewer large than small particles in materials subject to specific EU Regulation. However, these fewer, large particles often comprise the bulk of the mass.

A ‘minute piece of matter’ is only called a particle if this piece of matter has defined physical boundaries, i.e. if it can be distinguished from the surrounding matter. In other words: there must be, all around the particle, a continuous boundary that indicates where the particle ‘ends’. Also the word ‘interface’ can be used to describe this boundary. On the ‘other side’ of the boundary, there may be a continuous phase (gas, liquid, solid), or another particle.

Defined physical boundaries also separate crystallites in a polycrystalline solid material. These crystallites are called grains, and they are usually formed during solidification of a liquid cooled down below its melting temperature, or by recrystallization of an already solidified material. The presence of grains alone does not make these materials particulate materials, and therefore they do not fall in the scope of the EC NM definition. Such materials may be used as a basis for the preparation of nanomaterials, e.g. by milling or grinding. However, the pre-existing intergranular boundaries do not constitute ‘particle boundaries’. Only the external dimensions of the particles newly created in the comminution process are particle boundaries. In any case, for classification as nanomaterial the morphological identification of particles is needed. This identification may be difficult for a heavily sintered aggregate. In such cases, the knowledge of the production process can serve to distinguish polycrystalline materials (which are not nanomaterials) from heavily aggregated materials (which may be nanomaterials).

For the intended regulatory application of the EC NM definition, the term nanomaterial does not cover single molecules. This exclusion does not explicitly appear in the text of the EC NM definition, but it is mentioned in other EC documents [12, 15]. Single molecules are building blocks of many chemical substances and they are addressed in regulation independently of their size.

There is potential ambiguity for a number of specific cases:

- Fullerenes are well-defined molecules. Nevertheless they are explicitly included in the EC NM definition by derogation, together with graphene flakes and single wall carbon nanotubes with one or more external dimensions below 1 nm.
- Proteins are organic compounds consisting of one or more long chains of amino acid residues, sometimes comprising several subunits held together by hydrogen or other relatively weak bonds. Their shape and conformation can vary largely from one protein to the other, and a single protein may show quite different shapes and conformations depending on its environment. Very often, individual proteins have sizes above 1 nm.
- Macromolecules are 'very large molecules (organic or inorganic)' [16]. Polymers are macromolecules composed of many repeated subunits. As is the case with proteins, also individual macromolecules often have sizes above 1 nm.

Individual proteins, polymers and macromolecules are also excluded from the scope of the EC NM definition as they are considered single molecules. However, if these molecules are assembled into solid objects with clearly defined and stable external boundaries, and if they are stable enough to retain their shape over a longer period and to allow the measurement of their external dimensions, these objects should be considered as particles.

As the EC pointed out elsewhere [17], liquid or gaseous objects do not 'count' for the EC NM definition because the term 'particle' as used in the EC NM definition is intended to cover only entities with a defined rigid shape [17], thus in essence solid objects. The EC NM definition is therefore restricted to solid particles.

The term 'solid' has several meanings. It can describe an object that has no internal holes or pores, but this is not the intended use in the EC NM definition. For the Recommendation, 'solid' is one of the three classical physical states of matter, the others being liquid and gaseous. Most materials can exist in any of these three states, depending on the external conditions (temperature and pressure). In an attempt to describe certain materials the term 'soft material' is sometimes used, but this term is imprecise and does not have a clear definition. Therefore it should not be used in the context of the EC NM definition.

For an assessment of whether a material is a nanomaterial, particles should be solid at the normal temperature and pressure (NTP) of 25 °C (= 298.15 K) and 1 atm (= 101,325 Pa), see also e.g. [18].

The term 'solid' contrasts with the term 'fluid', which includes the liquid and gaseous states. Terms such as 'solid', 'liquid' and 'gaseous' are well known from daily experience and, for many materials in their bulk form, it is straightforward and more intuitive to classify them as solid or fluid in the following way:

- A classical criterion to distinguish a solid from a fluid is that a fluid continually deforms or flows under an applied shear stress. For a solid, if there is a deformation under applied constant shear stress, then the deformation stops after a certain time.
- A fluid, when placed in a container, conforms to the internal shape of the container.
- The atoms or molecules in a fluid do not have fixed (average) positions relative to each other, in contrast to a solid.
- In a solid, the atoms and molecules are linked by strong (ionic, covalent, metallic) bonds.

Criteria such as those listed above are in most cases sufficient to decide whether a bulk material is a solid. Solid nanomaterials are those for which the bulk (non-nano) form is solid. This excludes micelles, emulsions, aerosols of liquids and foams. The restriction to solid particles has the purpose to exclude from the EC NM definition highly dynamic objects, such as micelles or droplets in emulsions in general, including 'nano'-emulsions [19]. Solid materials have a certain rigidity or stiffness and they resist deformation which means that the particle retains its shape over a longer period. This

allows the measurement of their external dimensions, which is the basis of the EC NM definition.

From the above classification it is also evident that single molecules cannot be solid (nor liquid), because the classification can only be applied to ensembles big enough to form a phase for which the state (solid, liquid, gaseous) can be assessed. This is one reason why single molecules, with the exemptions discussed above, do not fall under the EC NM definition, as pointed out previously.

Particles should be solid

- A defined physical boundary (of a particle) is an 'interface'. Grains in polycrystalline materials are not to be considered as particles.
- The EC NM definition of a nanomaterial covers only particles that are solid at normal temperature and pressure (NTP), i.e. 298.15 K and 101,325 Pa.
- The term 'solid' should be understood in contrast to the liquid and gaseous states.
- Single molecules are not considered as particles in the EC NM definition with the exception of fullerenes, graphene and single-wall carbon nanotubes, which are explicitly included by derogation.
- The term 'soft material' should not be used in the EC NM definition context.

2.5 The term ‘material’

The term ‘material’ is not defined in current legislation; it is often used intuitively. An earlier JRC Report [13] discusses this term in the context of an overarching definition of nanomaterial. It was proposed that the term ‘material’ refers to a ‘*single or closely bound ensemble of substances at least one of which is in a condensed state (solid or liquid), where the constituents of substances are atoms and molecules*’. In the specific context of the EC NM definition, at least one of the substances must be solid.

The term ‘material’ is general since it should be usable independently from a specific regulation, and be adaptable to different sectors. It is a generic term for what is covered and regulated afterwards by sector-specific legislation. In this way it allows for straightforward and flexible amendment of specific legislation by using the EC NM definition with additional requirements according to sector-specific needs. Any non-particulate matter potentially associated with the particles in the same material (e.g. single molecules, impurities or stabilising liquid) in principle can be part of that material. If this is the case, non-particulate matter would not be considered in an assessment of

whether the material is a nanomaterial or not, because the external size of the particles are the sole determinant of the status of the material as nanomaterial.

This is also how the term ‘*containing*’ in the EC NM definition should be understood. This interpretation also ensures that the terms ‘material’ and ‘nanomaterial’ can be applied to what is covered in specific legislation, so that it is in line with existing legislation. For example, for the purposes of REACH *substances*, and for the purposes of the Cosmetics Regulation *ingredients*, are assessed to decide if they are nanomaterials or not. Whether only the particulate fraction of such a material, or the material as a whole, including e.g. stabilising liquid or reaction residues, is considered as nanomaterial, depends on how the EC NM definition will be implemented in specific legislation.

‘Material’ is a generic term

- The term *material* is generic and independent from specific legislation. In a specific regulatory context it can be replaced by what is covered and regulated by that sector specific legislation, e.g. substance, ingredient, etc.

2.6 External dimension (or ‘size’)

‘Particle size’, ‘average particle size’, or ‘particle size range’ are common and important parameters describing the ‘granulometry’ of powders and other particulate materials. The advantages of producing or using materials of small particle size are known since ancient times. However, the controlled reduction of particle size, or the controlled arrest of primary particle growth, to sizes in the range of what is now called the nanoscale (1 nm to 100 nm) is rather new for most materials. The size of a particle is now generally recognised as the main identifier for nanomaterials. Additional criteria are used in other definitions (such as a change in properties, compared to identical materials consisting of larger sized particles) [18], but always in combination with particle size.

The term ‘particle size’ is not very well defined. This is because the shape of particles is usually not a simple sphere (which is fully characterised with a single shape descriptor, e.g., the sphere diameter), but (much) more complex, resulting in many characteristic dimensions or ‘size aspects’. Particle size analysis techniques actually produce a particle size result as an ‘equivalent sphere

diameter’, which is the diameter of a virtual sphere that would create the same signal response in the size measurement process as a spherical particle of the same composition. Unless particles are perfectly spherical and solid, different measurement techniques can produce different ‘equivalent sphere diameter’ results when applied to the same particle.

In the discussions and consultations regarding characterisation of particles, the term ‘particle size’ is used abundantly. However, in the EC NM definition, which has to serve regulatory purposes, the term ‘external dimension’ is used instead. External dimensions are the dimensions that one can assess when assuming that the interior of the particle is solid, ignoring all internal structures. They can, for example, be represented as a Feret diameter (Figure 2.3) which is the distance between parallel tangents (e.g. aperture of a virtual caliper that is closed on the particle [20]), or as the diameter of the largest inscribed circle (circle that fits inside the particle profile) [21]. A detailed discussion of these terms can be found below in the section on irregular shapes.

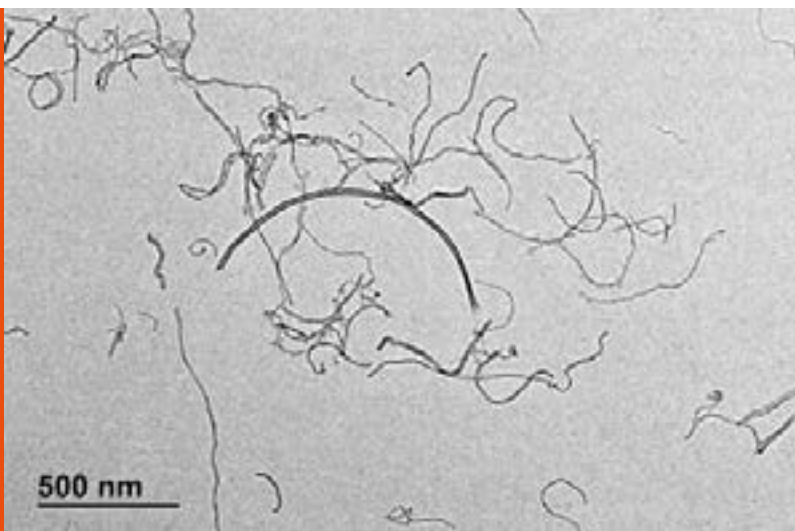


FIGURE 2.1

Fibres (elongated shapes) – multi-wall carbon nanotubes. In this case, the cross-sectional diameter is relevant for a correct assessment against the EC NM definition (TEM image by J. Ponti, Joint Research Centre, © European Commission)

When representing the ‘external dimension’ as a minimum Feret diameter, it is clear that every particle with a non-spherical or irregular shape has multiple ‘external dimensions’ which depend upon the orientation of the particle. The EC NM definition indicates that at least one of these external dimensions shall be in the range of 1 nm to 100 nm, for the particle to be contributing to the required 50 % of particles that qualify a material as a nanomaterial.

Particles with one of the three orthogonal external dimensions much smaller than the other two are often called plate-like particles (or ‘platelets’, when they are small) whereas particles with two external dimensions much smaller than the third are often called fibres or elongated particles.

In the case of very fine fibre-like or tubular particles, such as multi-wall carbon nanotubes (Figure 2.1), the length and shape of these tubes/fibres can be ignored when determining the size distribution. In most of the cases the appropriate dimension to be taken into account for a correct assessment against the EC NM definition will be their cross-sectional diameters.

Other materials consist of very thin plate- or flake-like particles, such as

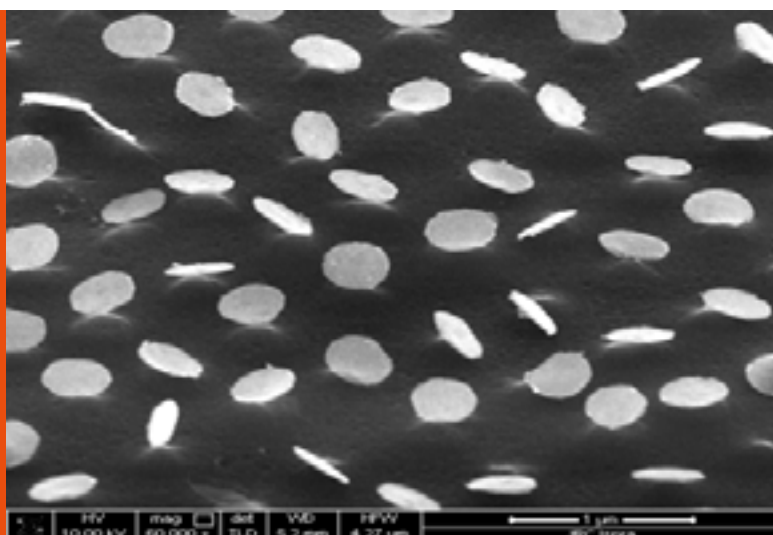
graphene flakes or clays. For such particles the appropriate ‘external dimension’ for application of the EC NM definition often is the average platelet/flake thickness (Figure 2.2).

In the above explanations and examples, the term Feret diameter has been used, because this size parameter is simple to visualise and understand, and it meets the requirements of the EC NM definition. The measured Feret diameter depends on the relative orientation of the particle and the virtual caliper. If one chooses to use the Feret diameter approach to establish a number size distribution, then the most relevant Feret diameter is the minimum Feret diameter, as it is the smallest possible Feret diameter when probed in multiple orientations. However, for the implementation of the EC NM definition, it is not always necessary to establish the minimum Feret diameter of each particle. In fact, any Feret diameter value below 100 nm is sufficient to show that the particle has at least one external dimension < 100 nm.

Another useful size parameter is the maximum inscribed circle diameter: it is the diameter of the largest circle that fits inside the virtual envelope of the boundaries of the particle on a 2D image.

FIGURE 2.2

Plate-like shapes: Au “nanocoins” on polymer substrate
(SEM image by A. Valsesia, Joint Research Centre,
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The minimum Feret diameter and the maximum inscribed circle (or sphere) diameter are direct assessments of the external dimensions of particles on which the nanomaterial definition is based. Which of these quantities should be used to assess the external dimensions of irregularly shaped particles for the EC NM definition depends on other shape parameters. One possibility is to use the minimum Feret diameter and the maximum inscribed circle diameter if the solidity^d of the particle shapes falls within certain ranges; see also Figure 2.3. It is in any case necessary to measure the external particle dimensions in such a way that an assessment of the material against the EC NM definition is possible.

Particle size analysis techniques provide 'equivalent sphere' or 'equivalent circle' diameters (Figure 2.4). These parameters are overestimations of the minimum external dimension and have to be used cautiously, as they may result in false negative classification, i.e. classifying a material as non-nanomaterial when in

fact it is a nanomaterial. It is for example not meaningful to measure the smallest external dimension of a nanotube with a technique providing an equivalent sphere diameter.

Nevertheless, the methods to measure equivalent sphere and equivalent circle diameters have their merits as well. In particular, when it can be shown, or when it is known, that the solidity^d of a particle is high (meaning that the particle has a compact geometry, cf. Figure 2.3, then the measured values of equivalent sphere and equivalent circle diameters can be used as estimates of the smallest external dimension. One only needs to be aware that the measured value is almost always an overestimate.

More detailed information on this subject is elaborated in the JRC's follow-up report on that subject, where criteria are suggested to help choosing appropriate size parameters and size analysis methods.

^d According to ISO 9276-6:2008, solidity is a measure of the overall concavity of a particle: $Solidity = A/A_c$, where A_c is the area of the convex hull (envelope) bounding the particle, and A is the projected area.

Feret_{min} LARGEST INTERNAL CIRCLE SOLIDITY

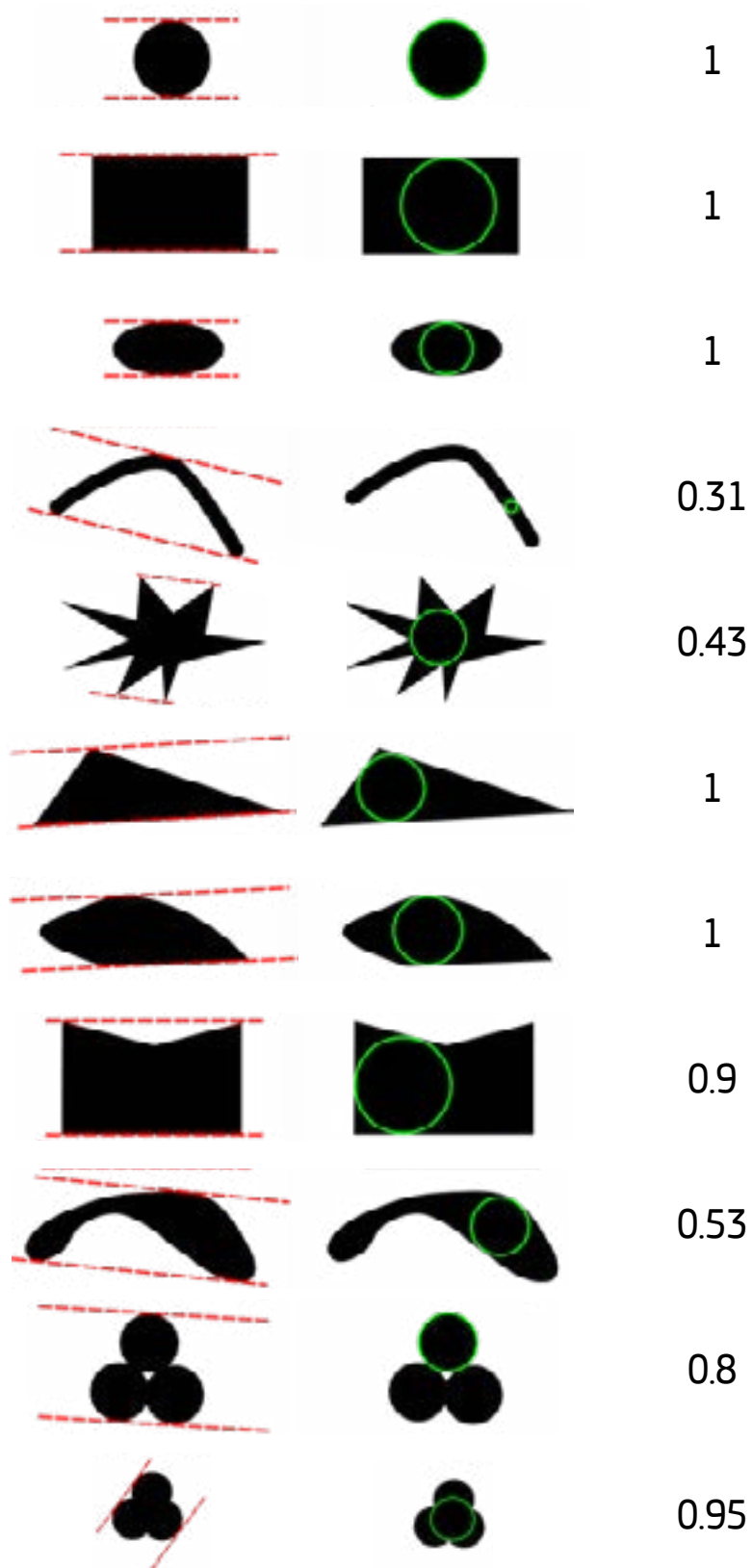


FIGURE 2.3

Illustration of different particle shapes and morphological parameters (two-dimensional projections). The last two shapes at the bottom represent agglomerates and aggregates respectively. There the minimum Feret diameter (Feret_{min}) refers to the entire agglomerate/aggregate, whereas the maximum inscribed circle does not refer to the entire aggregate, but to the constituent particles of the agglomerate/aggregate (from the NanoDefine project [21]). The consequences for measurements will be discussed in the JRC's follow-up report on that subject.

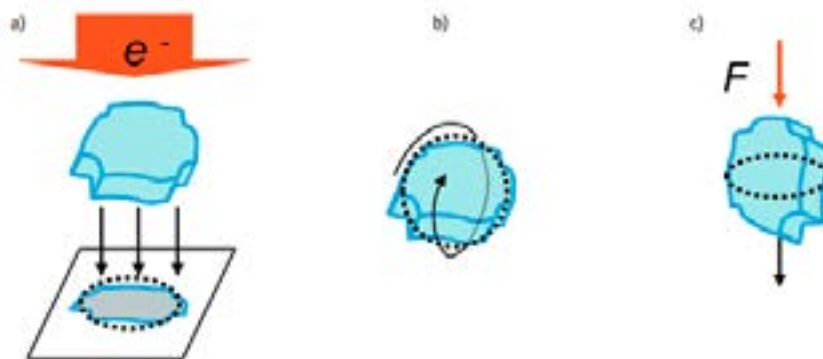


FIGURE 2.4

Illustration of the concept of equivalent diameter:
 a) diameter of a circle causing the equivalent electron-shadow area;
 b) diameter of a sphere that has the same rotational inertia
 c) diameter of a sphere that would sediment due to a gravitational force F with the same speed as the particle. All three diameters are different, as they correspond to different aspects of the particle behaviour and properties (from [20]).

External dimensions of particles

- The term 'particle size' is often used in the context of nanomaterial definitions, although it is not well defined if the particles are not spherical. The EC NM definition uses the more precise term 'external dimension'.
- Many particle size analysis techniques produce equivalent spherical particle diameters and tend to overestimate the minimum external dimensions.
- External dimensions can be represented in various ways, e.g. by the Feret diameter.
- The external dimensions of particles with irregular shape can be assessed by the minimum Feret diameter and/or the maximum inscribed circle diameter.

2.7 The terms ‘agglomerate, aggregate and identifiable constituent particle’

Agglomerates and aggregates are particles made up of smaller particles, called ‘constituent particles’. Constituent particles are the (morphologically) identifiable particles inside an aggregate or agglomerate:

- In agglomerates the constituent particles are only weakly bound. Constituent particles are usually not deformed during an agglomeration process.
- In aggregates the constituent particles are strongly bound. This is often the result of a high-temperature process during which constituent particles fuse together. This fusion process results, to a varying extent, in a deformation of the constituent particles, to the point of their disappearance as distinguishable structures.

It should be noted that the term ‘primary particle’, which is not used in the EC NM definition, is nevertheless often used in this context in an incorrect way. Primary particles are the original seeds from which particles grow and are therefore an unrelated concept to constituent particles, aggregates and agglomerates. Therefore, the term ‘primary particle’ is irrelevant for the EC NM definition.

There are a number of particle characterisation instruments that can in many cases provide information about, and access to, the constituent particles, most of which are microscopy-based techniques. Other particle size analysis methods are often based on measuring a particular kind of mobility of particles. Since aggregates and agglomerates

move as a unit, their mobility behaviour cannot be related mathematically to the external dimensions of their constituent particles. Mobility-based techniques therefore cannot be used to measure the size of constituent particles in aggregates and agglomerates. More detailed information on this subject will be given in the JRC’s follow-up report on that subject.^e

The difference between agglomerates and aggregates is determined by the strength of the bonds between their constituent particles. Aggregates and agglomerates themselves can also interact and form larger agglomerates/aggregates. The secondary structure of this mix of aggregates and agglomerates can be complex and dynamic: the number of constituent particles in one larger unit can change rapidly, especially in agglomerates. This is the main reason why the EC NM definition is based on the size of the constituent particles, which is a more stable feature of a nanomaterial, even if the size of constituent particles may be sometimes difficult to measure. Therefore, while the implementation of the EC NM definition does not require distinguishing between aggregates and agglomerates, the difference between aggregates and agglomerates has a number of consequences for the selection of suitable measurement methods, which will be discussed in the JRC’s follow-up report on that subject.

Agglomerates, aggregates and constituent particles

- Constituent particles are the morphologically identifiable particles inside an aggregate or agglomerate.
- Agglomerates consist of weakly bonded constituent particles.
- Aggregates consist of strongly connected ('fused') constituent particles.
- Mobility-based techniques cannot be used to measure the size of constituent particles in aggregates and agglomerates.
- For the implementation of the EC NM definition it is not necessary to distinguish between aggregates and agglomerates. The determining factor is the external dimension of the constituent particle.

2.8 Particle number-based particle size distribution

As indicated earlier, the term ‘number size distribution’ is a short phrase for ‘particle number-based (or -weighted) particle size distribution’.

The simplest representation of a number size distribution is a histogram, which is a graph that shows how the size of particles in a powder, or in dispersion, is distributed between a lowest and a highest size value. Typically, the abscissa (x-axis) corresponds to the particle size information, and the ordinate (y-axis) shows the information on the number of particles of a certain size. To construct the histogram (Figure 2.5), particles are grouped in ‘bins’ (small sections or particle size intervals on the x-axis).

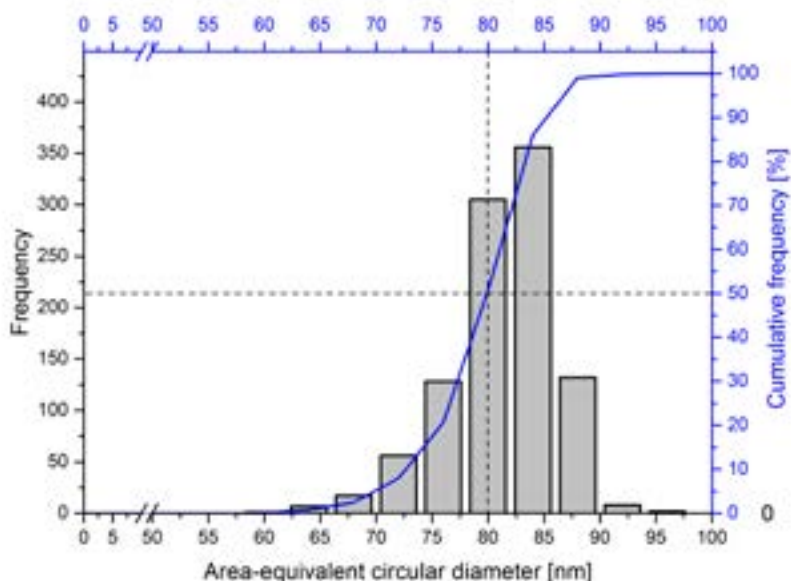
Particle size data are also often represented as a cumulative distribution (Figure 2.5, blue line), which can be deduced from the information shown in a histogram. The cumulative distribution is very convenient to determine the median value, $x_{50,0}$, of the number size distribution (from the intersection of the two dashed lines in Figure 2.5). It is the size of the particles that divides the particle population in two groups of an equal

number of particles. One group contains all particles smaller than the median size and the other group all those larger than the median size, $x_{50,0}$.

For a number size histogram, the amount of particles in each size bin is simply the number of particles in the bin. This corresponds with the most direct way of counting particles, for example with a microscope. However, most other particle size analysis techniques produce other types of size distributions, based on the raw or converted measured signal produced by the particles of a certain size. This signal can be proportional to their mass, or to their surface area, or to the intensity of their scattered light, or a range of other parameters, usually covered with the term ‘intensity’. It is generally not straightforward, and usually significantly amplifies errors, to transform the resulting ‘mass size distribution’ or ‘surface area size distribution’ or ‘scattered light intensity size distribution’ into a ‘number size distribution’ [20,23]. Only in the case where the shape and material properties of the particles are regular, accurately known and do not vary

FIGURE 2.5

Particle size distributions for the certified reference material ERM-FD101b by TEM: histogram (grey) and cumulative distribution (blue line) (from [22]). The median value of the number-based size distribution ($x_{50,0}$) is given by the intersection of the two dashed lines. In this example it is 80 nm.



between particles and where the initially measured size distribution is known with sufficient precision (sufficient number of size bins, sufficient number of particles per size bin) and where the difference in size between largest and smallest particles is small, can such transformations lead to reliable number size distributions.

The EC NM definition follows the logic that for a material to be classified as 'X', the majority of constituents must be of class 'X'. In the EC NM definition, the metric used is the particle number fraction of particles with external diameters

between 1 nm and 100 nm. Following that logic, the requirement arises that for a material to be a nanomaterial, more than half (50 %) of the particles of which the material consists must meet certain size requirements.

It should be noted that a particle fraction of 50 % with one or more external dimensions smaller than 100 nm in a number size distribution is always less than 50 % in any other usual size distribution metric, such as volume or mass. In fact it can correspond to a tiny fraction of the total mass of the material.

The 50 % threshold criterion

- If 50 % or more of the particles of a material in the number size distribution have one or more external dimension in the size range 1 nm to 100 nm, then the material is a nanomaterial.
- The fraction of particles with one or more external dimensions in the size range 1 nm to 100 nm can (depending on the details of the particle size distribution) be a tiny fraction of the total mass of the material and at the same time be a majority in the total number of material particles.
- 50 % of particles with one or more external dimensions smaller than 100 nm in a number size distribution are always less than 50 % in any other size distribution metric, such as surface, volume or mass.

2.9 Nanomaterials in products

A variety of products are regulated in the EU under product-specific legislation. Some of these products contain or have been produced with nanomaterial ingredients and some of them may also have internal structures or surface components in the nanoscale, for example coatings or computer chips.

The EC NM definition is not intended to cover solid products as defined in EU regulation [24] or components, even if they contain nanomaterials or have an internal structure at the nanoscale. The EC NM definition applies only to the nanomaterial in terms of particulate matter itself and not to the resulting product of a combination of (a) nanomaterial(s) with other components. When identifying a material as a nanomaterial or not, the material, and not the final product integrating the material, should be assessed. Therefore, a consumer product or an end product is not a nanomaterial itself if it contains nanomaterial(s) as component(s). Accordingly, a tyre or a cosmetic product, for instance, does not become a nanomaterial itself, if it contains a nanomaterial ingredient.

Thus, even if a product contains one or more nanomaterials as components, or if it is designed to release nanomaterials, or releases nanomaterials as wear debris during use or ageing, it is not a nanomaterial itself. This also means that the criterion that a material is a nanomaterial if 50 % or more of the particles have one or more dimensions in the range of 1 nm to 100 nm should be applied only to the material itself, and not to a product or parts of it that contain the material, unless the product is a particulate material itself.

It should be noted that identifying an ingredient of a product as nanomaterial does not allow any conclusions on the actual concentration of particles with one or more dimensions in the range 1 nm to 100 nm in that product. For this, one needs to know (i) the complete quantitative composition of the product and (ii) the complete number size distribution of the ingredient.

Products containing nanomaterials

- The EC NM definition does not cover (consumer) products or components in which nanomaterials are integrated.
- Even if a product contains nanomaterials, or when it releases nanomaterials during use or ageing, the product itself is not a nanomaterial, unless it is a particulate material itself that meets the criteria of particle size and fraction.

2.10 Volume Specific Surface Area

The Recommendation (2011/696/EU) includes a criterion based on volume specific surface area (VSSA). If VSSA can be measured and if requested in specific legislation, then compliance with the EC NM definition can be determined on the basis of the VSSA – if $VSSA > 60 \text{ m}^2/\text{cm}^3$, then the material should be considered a nanomaterial.

As VSSA can only be used if requested in specific legislation, it cannot be considered as a criterion that is equivalent to the 50 % threshold in the number distribution. Assessment of whether a material falls under the EC NM definition should preferentially be done by analysing the number distribution. If specific legislation allows using VSSA to identify nanomaterials there are certain scientific-technical considerations that should be taken into

account. These are briefly summarised below, and they will be discussed in more detail in the JRC's follow-up report on that subject.

Under certain conditions it is possible to use VSSA in conjunction with other threshold values and combined with other techniques or evidence, as a proxy to the precise determination of the number size distribution to decide if a material is a nanomaterial or not. Methods for the experimental determination of the VSSA based on the Brunauer, Emmett and Teller (BET) method are widely available and relatively simple to apply, provided that the BET method is used within its range of validity, as described in the ISO 9277 standard for the determination of the specific surface area of solids by gas adsorption [25].

2.10.1 Specific Surface Area and Volume Specific Surface Area

The specific surface area (SSA) of a particulate material (in m^2/g) is derived from the value of the surface area SA (in m^2) of a powder sample and its mass m (in g): $SSA = SA/m$. The International Union of Pure and Applied Chemistry (IUPAC) defines the SSA in the following way: *'When the area of the interface between two phases is proportional to the mass of one of the phases (e.g. for a solid adsorbent, for an emulsion, or for an aerosol), the specific surface area [...] is defined as the surface area divided by the mass of the relevant phase'* [26].

In 2010, ISO published a revised standard for the experimental determination of the overall SSA of either powders or porous solids by measuring the amount of physically adsorbed gas according to the BET method [25]. The overall SSA includes all accessible internal and external surfaces. While SSA can be determined by other methods, BET remains by far the most

commonly used method both in research and industry laboratories. The EC NM definition specifically mentions BET as a method for measuring SSA, but it does not exclude other methods. Often, N_2 is the probe gas (adsorptive) of choice, but other gases, such as Ar, can be used as well. Interlaboratory comparisons on nanomaterials [27,28], have demonstrated that BET measurements can be reasonably reproducible.

The VSSA is very similar to the SSA; the only difference is that the surface area is normalised against the volume of the powder sample instead of its mass. One can therefore adjust the IUPAC definition of SSA to obtain the following definition for VSSA: *when the area of the interface between two phases is proportional to the volume of one of the phases (e.g. for a solid adsorbent, for an emulsion or for an aerosol), the volume specific surface area, or VSSA, is defined as the*

surface area SA divided by the volume V of the relevant phase: $VSSA = SA/V$. For a non-porous particulate material this means that the VSSA is equal to the sum of the surface areas sa_i of all the particles divided by the sum of the volumes v_i of all the particles [29], and also that $VSSA = SSA \times \rho$ where ρ is the material density.

Thus:

$$VSSA = \frac{SA}{V} = \frac{\sum_i sa_i}{\sum_i v_i} = SSA \times \rho \quad (1)$$

The density value used to convert SSA to VSSA is the (average) density of the 'relevant phase'. For example in the case of a solid non-porous TiO_2 powder, the density value used to convert the SSA to VSSA should be the density of the TiO_2 phase, not the overall 'bulk powder density'. In practice, the density value used is often the 'skeletal density' as determined by the helium pycnometry method [30,31]. In many cases this will be equal or close to the known 'true density' available for most materials, for example, in

the Handbook of Chemistry and Physics [32]. It should be noted that open particle porosity (particles have pores not totally enclosed by their walls and open to the surface either directly or by interconnecting with other pores), while increasing the surface area and decreasing overall particle density (or 'envelope density'), do not in principle affect the skeletal density. The latter is affected if there is a significant volume fraction of non-gas-accessible voids (or 'closed pores') present within the particles [30]. It may be argued that this would be unlikely for very fine particulate materials. The JRC's follow-up report on that subject will further discuss density values to be used when converting SSA to VSSA.

It is possible to estimate the VSSA from transmission electron tomography studies [33] for non-porous, non-aggregated particles that have a reasonably uniform shape and size, but this method is highly impractical or unfeasible for materials consisting of porous or very irregularly shaped particles.

2.10.2 Relationship between particle size distribution and VSSA

For the simplest case of an ideally monodisperse (all particles have the same size) particulate material consisting of perfectly spherical non-porous particles of diameter D (in nm), the VSSA (in m^2/cm^3) is given by: $VSSA = 6000/D$.

Broadening a monodisperse number size distribution to a Gaussian (normal) or lognormal distribution, but maintaining monomodality (a single peak in the particle size distribution), while keeping the median value of the distribution fixed, leads to a reduction in the overall sample VSSA. Figure 2.6 illustrates this for the case of a lognormal size distribution.

One can notice that the VSSA is reduced appreciably by broadening the particle size distribution (PSD), although in order to achieve a large reduction in VSSA, the

PSD needs to be quite strongly broadened, and this is accompanied by a significant reduction in the mass of particles having a diameter below 100 nm.

For multimodal PSDs (there are several peaks in the graphical representation of number vs size), where there is a significant size difference between modes, the VSSA is in general dominated by the larger size mode(s). A simple example has been published for the case of a perfectly bimodal sample with 2/3 of the particles being 10 nm in diameter and 1/3 being 500 nm in diameter [29]. The overall VSSA of such a sample is $12.01 m^2/cm^3$, which within experimental error is equal to the VSSA of the larger mode alone, $12 m^2/cm^3$. This example shows that using VSSA as the sole

criterion to identify materials, without any knowledge of shape or particle size distribution would often give false results. This is one reason why the VSSA criterion *may only be applied to positively*

identify nanomaterials if the VSSA value is above $60 \text{ m}^2/\text{cm}^3$, and may not be used to categorise materials as 'non-nanomaterials'. This is discussed in more detail in the next section.

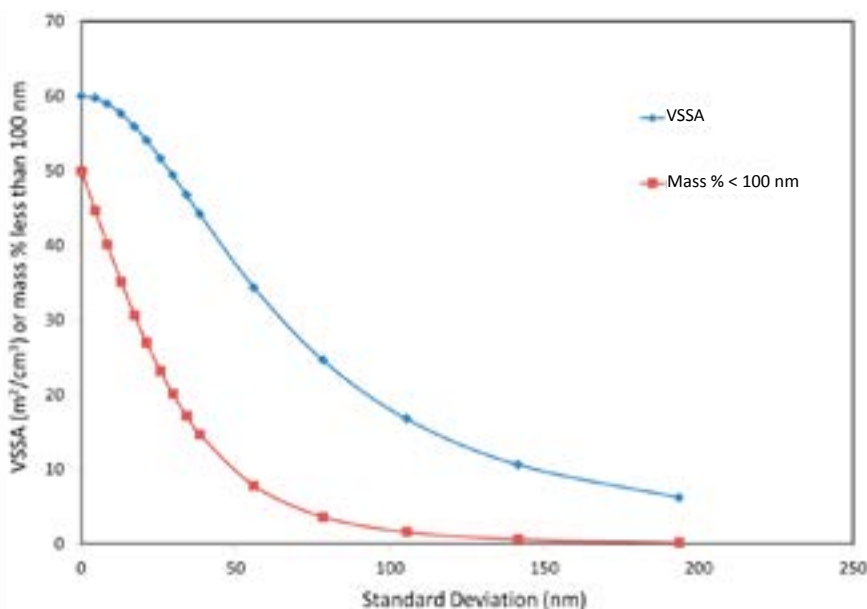


FIGURE 2.6

Variation of VSSA (blue line) as a function of the standard deviation for a lognormal particle size distribution (perfectly spherical and non-porous particles) with a median particle size of 100 nm. The calculated variation of the mass % of nanoparticles below 100 nm (red line) is also shown.

2.10.3 Using VSSA to identify nanomaterials

The EC NM definition includes an upper VSSA value of $60 \text{ m}^2/\text{cm}^3$ for *positive* identification of nanomaterials. This value corresponds to the VSSA of a perfectly monodisperse sample of non-porous spherical particles with a particle diameter of 100 nm. The widely available, relatively simple and reproducible BET method can be used to determine the VSSA^f.

A more in-depth discussion of the effects of particle shape and size distribution will be presented in the JRC's follow-up report on that subject. However, we can note that factors such as PSD broadening (as outlined in the last section), changing the particle shape to non-spherical [5,31] and particle aggregation tend to reduce VSSA (for a fixed median minimum external dimension), and the VSSA

of multimodal samples is generally dominated by the larger size modes where the particle numbers in the modes are not too dissimilar. The only likely factors (assuming non-exotic particle shapes) that might increase VSSA while maintaining the same external dimensions would be increasing particle porosity or surface roughness.

These facts mean that if a VSSA above $60 \text{ m}^2/\text{cm}^3$ is measured for a sample that is known to consist of non-porous, relatively smooth, solid particles, then in all likelihood that sample will be a nanomaterial also according to the size-based criterion. On the other hand, if a VSSA of less than $60 \text{ m}^2/\text{cm}^3$ is measured, one cannot logically conclude that the sample is not a nanomaterial according to

^f For certain surfaces the use of Ar instead of N_2 is recommended. Ref. [25] provides more information on the use of specific probe gases (adsorptives).

the size-based criterion. Arguments in favour of using VSSA as a criterion to positively identify nanomaterials are also discussed elsewhere [12,34]. It is also argued in those works that because particle porosity and excessive surface roughness increase VSSA, the VSSA criterion can lead to a so-called 'false positive' classification in some cases.

It is now apparent that for a practical implementation of the EC NM definition, VSSA is much more powerful when combined with complementary techniques in order to draw logical conclusions as to

whether a sample falls under the size-based criterion or not [31]. This is expanded in the JRC's follow-up report on that subject. In general, assessment of a material against the EC NM definition according to the number based distribution overrules assessment according to the VSSA.

The VSSA should be measured by applying reliable and standardised methods [31]. This is discussed in the second JRC report on this topic, which also takes into account the approach and the results from the NanoDefine project [31].

VSSA of nanomaterials

- For a particulate material the VSSA is equal to the sum of the surface areas of all particles divided by the sum of the volumes of all particles:

$$VSSA = \frac{SA}{V} = \frac{\sum_i sa_i}{\sum_i v_i} = SSA \times \rho$$

- The VSSA of a sample can be calculated if the particle size distribution and the particle shape(s) are known in detail. The reverse (calculating the size distribution from the VSSA value) is unfeasible.
- For a given median diameter, an increase in polydispersity tends to reduce the VSSA.
- 50 % by number may equate to much less than 50 % by mass for polydisperse samples.
- $VSSA > 60 \text{ m}^2/\text{cm}^3$ is likely to be a reliable indicator that a material is a nanomaterial unless the particles are porous or have rough surfaces.
- Many nanomaterials (according to the principal size-based criterion) will have a VSSA of less than $60 \text{ m}^2/\text{cm}^3$.
- The $VSSA > 60 \text{ m}^2/\text{cm}^3$ criterion can only be used to show that a material is a nanomaterial, *not vice versa*.

3 Other issues to be considered

The reliable measurement of $x_{50,0}$ (the median size in the particle number size distribution that determines whether a material is a nanomaterial or not) of non-spherical and/or agglomerated/aggregated constituent particles in the nanoscale is an analytical challenge. Several particle size measurement methods exist, even if not all of them were developed to measure an $x_{50,0}$ value. To assess results obtained with different methods it is necessary to understand that the obtained particle size values are 'method-defined'. The measured size values not only depend on the test material, but also on the method, including data evaluation approaches [35]. Therefore, a short statement, such as ' $x_{50,0} = 37 \text{ nm}$ ', is usually not sufficient to understand the correct and full meaning of the measurement result, and to use it in the assessment of the EC NM definition. Specific guidance on this subject is needed. This was recognised by the EC and as a result the EU FP7 NanoDefine research project was funded [39].

The second JRC report on this subject will provide detailed information on the current possibilities for reliable assessment of materials against the quantitative criteria in the EC NM definition. The document will be partly based on the outcome of the NanoDefine project, as well as on the findings of other studies in the particle size analysis field. The main topics that will be treated in the JRC's follow-up report on that subject are listed and briefly explained here:

Good measurement practice

Interpretation problems and disputes over reported measurement results can only be solved if the measurement laboratories adhere to the generic good

measurement practices, such as the validation of the methods they use and a detailed documentation and reporting of all relevant steps in the measurement process. This is the basis of quality management standards for laboratories, such as the ISO/IEC 17025 'General requirements for the competence of testing and calibration laboratories' developed by ISO and the International Electrotechnical Commission (IEC) [36], or the Principles of Good Manufacturing Practice [37], and Good Laboratory Practice (GLP) developed under OECD [38].

The rigorous and full implementation of good measurement practice including the requirements of ISO/IEC 17025 [36] is sometimes regarded as cumbersome and is argued to slow down the more creative steps in the early stages of developing new measurement methods and new products. However, good measurement practice is not a rigid procedure, its requirements allow for flexibility. For example, according to ISO/IEC 17025 validation of a method shall be '*as extensive as is necessary to meet the needs of the given application or field of application*'. In addition, well-maintained instruments, trained staff, documented methods and proper reporting is a prerequisite for any measurement result to be meaningful. The JRC's follow-up report on that subject will provide further information on how to address these issues and how to perform measurements on nanomaterials in a way that is suitable for use in a regulatory context.

Sample preparation

An important element in most analytical processes is the preparation of samples which are representative for the entire material. This is especially the case for nanoparticle size analysis, because of the intense interaction between nanoparticles (aggregation, agglomeration). Some particle size analysis methods are, under certain conditions, capable of distinguishing constituent particles in an aggregated or agglomerated form (e.g. electron microscopy), and are less affected by this problem. However, nanoparticles also have a tendency to adsorb or deposit on other, larger particles or on external surfaces. This can lead to selectivity problems and resulting errors, also with microscopy methods. In any case, sample preparation is a major challenge for all other methods. For these methods, sample preparation steps must not only be listed, but also timed to capture the dynamics of any possible agglomeration processes.

Measurement methods for particle size analysis

In 2012, the JRC [20] produced a first overview of the candidate methods for the implementation of the EC NM definition, including an assessment of their limitations. The JRC's follow-up report on that subject will provide an update of that information. An important contribution to this update is the outcome of the NanoDefine project [31,39,40].

NanoDefine decision support flow scheme

The implementation of the EC NM definition, across all sectors, legislations and nanomaterial types, will not rely on the use of a single method. Even assessments of individual materials will often rely on the results obtained with two or more measurement methods. This calls for the use of an integrated, tiered approach in decision support flow schemes. The recommended decision support scheme draws largely on the

scheme developed in NanoDefine. This is elaborated and discussed in the JRC's follow-up report on that subject, together with the corresponding NanoDefiner e-tool, which implements the tiered decision support system in a user-friendly software [41]. The report also contains a discussion on the role that can be played by measurements of (V)SSA [31] - in combination with other techniques - as a proxy to show that a material is not a nanomaterial and in the identification process of nanomaterials.

Reference measurement systems: documentary standards, proficient laboratories and reference materials

Ultimately, the implementation of the nanomaterial definition will benefit from a complete and reliable reference measurement system. Such a system does not only depend on the availability of the validated methods mentioned above. The basis of a robust measurement system is threefold.

The first pillar is that of validated, ideally standardised, test methods. These are methods for which a full description of the method is documented and agreed upon and whose performances have been demonstrated to be fit for purpose. Available standard methods are described in the JRC's follow-up report on that subject. Many of the available documentary standards may be relevant, but usually they are not specifically designed for the implementation of the EC NM definition. Often, they only provide generic guidelines on how to implement a specific measurement technique.

The second pillar is a sufficient number of laboratories that are proficient in the use of the standard methods. Regular participation in proficiency tests can help laboratories to demonstrate, for themselves and for third parties, e.g. accreditation bodies, that they master the methods. The follow-up report will provide examples of organisations and networks that

are active in the area of proficiency tests and accreditation.

The third pillar of a reference measurement system is formed by reference materials. They are used in several ways in the process of analytical quality assurance. Reference materials are indispensable when establishing the reproducibility of a method, or when setting up a proficiency test. Certified reference materials are used for calibration, or for the in-house tests in a laboratory that wants to check whether it is correctly implementing a standard method. The follow-up report provides a snapshot of the already available certified reference materials, and explains the status and use of non-certified reference materials and representative test materials.

Measurement uncertainty: examples and case studies

If measurements are made within a reference measurement system, then it is possible for the analyst to associate and report with each measurement result a reliable measurement uncertainty. This information is, for example, essential if a measurement result is intended to be compared against a regulatory limit or threshold. The practical implementation and estimation of measurement uncertainty is not always straightforward. Therefore, the JRC's follow-up report on that subject gives some examples and case studies, to illustrate the concept and to explain some of the possible practical approaches to this issue.

Reliable identification of nanomaterials

- Suitable sample preparation, appropriate measurement methods, a robust reference system and an integrated decision flow scheme are key elements for a reliable identification of nanomaterials.

4 Conclusions

This report addresses the basic elements of the EC NM definition, the origin of the material, the distinction between nanomaterials and nanostructured materials, the terms 'particle', 'constituent particle' and 'material', external particle dimensions, particle size distribution and the volume specific surface area.

- The EC NM definition is horizontal and not sector-specific. It is a Recommendation and is thus not legally binding. It is generally in line with other approaches worldwide, but it is more specific and quantitative than most other definitions. This enables its implementation in a regulatory framework.
- The EC NM definition is based on the only feature that is common to all nanomaterials: their nano-scale external dimensions. It categorises a material by the fraction of its constituent particles in a defined size range, measured on the basis of the particle number-based particle size distribution.
- The EC NM definition applies to all materials regardless of their origin. Nanomaterials are not necessarily hazardous and a definition based only on size properties cannot differentiate between hazardous and non-hazardous materials.
- The EC NM definition covers only particles that are solid at normal temperature and pressure (NTP), i.e. 298.15 K and 101,325 Pa.
- The EC NM definition is a definition of 'nanomaterial' and not 'nanostructured material'. The latter is generally taken to include materials that have nanoscale internal or surface structures, whereas the EC NM definition is only based on particle external dimensions. Some nanostructured materials may fall under the definition if they are particulate and external particle size criteria are met.
- A 'particle' is a minute piece of matter with defined physical boundaries (interfaces). Grains in polycrystalline materials are not to be considered as particles.
- Single molecules are not considered as particles in the EC NM definition with the exception of fullerenes, graphene and single-wall carbon nanotubes, which are explicitly included by derogation.
- The term material is generic and independent from specific legislation. In a specific regulatory context it can be replaced by what is covered and regulated by that sector specific legislation, e.g. substance, ingredient, etc.
- External particle dimensions can be represented in various ways. With regard to the EC NM definition, the external dimensions of particles with irregular shape should normally be assessed by the minimum Feret diameter and/or the maximum inscribed circle diameter. This will be expanded in the JRC's follow-up report on that subject.

- Many particle size analysis techniques produce equivalent spherical particle diameters and tend to overestimate the minimum external dimensions.
- Constituent particles are the morphologically identifiable particles inside an aggregate or agglomerate. For the implementation of the EC NM definition it is not necessary to distinguish between aggregates and agglomerates
- Mobility-based techniques cannot be used to measure the size of constituent particles in aggregates and agglomerates.
- The 50 % threshold criterion for a nanomaterial refers to the number size distribution. If 50 % or more of the particles of a material in the number size distribution have one or more external dimensions in the size range 1 nm to 100 nm, then the material is a nanomaterial.
- The fraction of particles with one or more external dimensions in the size range 1 nm to 100 nm can (depending on the details of the particle size distribution) be a very small fraction of the total mass of the material and at the same time be a majority in the total number of material particles.
- 50 % of particles with one or more external dimensions smaller than 100 nm in a number size distribution are always less than 50 % in any other normally-used size distribution metric, such as surface, volume or mass.
- Even if a product contains nanomaterials, or when it releases nanomaterials during use or ageing, the product itself is not a nanomaterial, unless it is a particulate material itself that meets the criteria of particle size and fraction.
- In a particulate material, the volume specific surface area (VSSA) is equal to the sum of the surface areas of all particles divided by the sum of the volumes of all particles.
- The VSSA of a sample can be calculated if the particle size distribution and the particle shape(s) are known in detail. The reverse (calculating the size distribution from the VSSA value) is unfeasible.
- $VSSA > 60 \text{ m}^2/\text{cm}^3$ is likely to be a reliable indicator that a material is a nanomaterial unless the particles are porous or have rough surfaces, but many nanomaterials (according to the principal size-based criterion) will have a VSSA of less than $60 \text{ m}^2/\text{cm}^3$.
- The $VSSA > 60 \text{ m}^2/\text{cm}^3$ criterion can only be used to show that a material is a nanomaterial, not vice versa.
- Suitable sample preparation, appropriate measurement methods, a robust reference system and an integrated decision flow scheme are key elements for a reliable identification of nanomaterials.

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Abstract

This report supports the implementation of the European Commission's Recommendation on a definition of nanomaterial (2011/696/EU). It addresses its key concepts and terms and discusses them in a regulatory context. Corresponding to the broad scope of the definition the considerations in this report can be applied across all relevant legislative areas; they are not specific to any particular piece of legislation. The report provides recommendations for a harmonised and coherent implementation of the nanomaterial definition in any specific regulatory context at European Union and national level.

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