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Considerations on a Definition of Nanomaterial for Regulatory Purposes

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Contact information
IHCP Communication Office
jrc-ihcp-communication@ec.europa.eu
IRMM Communication Office
jrc-irmm-info@ec.europa.eu

http://www.jrc.ec.europa.eu/

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Executive summary

The term ‘nanomaterial’ is now frequently used for a variety of materials. It usually refers to materials with external dimensions, or an internal structure, measured in nanometres that exhibit additional or different properties and behaviour as compared to coarser materials with similar chemical composition. Nanomaterials are now used in many innovative technological applications and products, including a wide range of consumer products, and there is growing concern about their safe use and possible impact on human health and the environment.

In a European Parliament resolution from 2009 it is questioned whether, in the absence of any nanomaterial specific provisions, Community legislation covers all relevant risks related to nanomaterials. The European Parliament also called for, inter alia, a comprehensive science-based definition of the term ‘nanomaterial’. The aim of this report is to review and discuss issues and challenges related to a definition of ‘nanomaterial’, and to provide practical guidance for a definition for regulatory purposes.

The report suggests that a definition for regulatory purposes should:

- only concern particulate nanomaterials,
- be broadly applicable in EU legislation, and in line with other approaches worldwide,
- use size as the only defining property.

This calls both for a clarification of the meaning of the word ‘material’ and a clear definition of the nanoscale limits. Enforceability of the definition requires the adoption of instructions on how such limits can be applied for nanoscale materials with size distributions. Size-derived properties, nanoscale materials incorporated in a matrix and the origin of the material are also points that should be considered.

It is clear that any definition will have implications within the context in which it is used and may need adaptation for specific regulations or directives. It should therefore be emphasised that adoption of a definition will also involve policy choices, and accordingly will entail political decisions.

1. Introduction

The introduction of new technologies often creates new challenges for the legislator, particularly if the associated consumer products, in addition to the expected benefits, raise concerns about health and environmental risks. In this case, new regulations or the adaptation of the existing ones may be required, and the regulatory authority has to define what needs to be regulated.

Nanotechnology holds considerable promise in many different technological areas and industrial sectors. Many nanotechnology applications are based on novel as well as conventional materials deliberately engineered to be nanostructured, for which the term 'nanomaterial' is now frequently used. The term broadly refers to materials with internal structures and/or external dimensions within the size range measured in nanometers (nm) where 100 nm is frequently used as a delimiting size between the nanoscale and the micro and macroscopic scales. In the nanoscale regime, some materials exhibit additional or different features or properties as compared to coarser materials with similar chemical composition. These materials are now used in a wide range of innovative technological applications and products, including many consumer end-products.

While there are today many nanotechnology products being introduced onto the market, there is also a considerable lack of knowledge concerning the biological effects and environmental impact of nanomaterials. This has triggered an increasing worldwide effort to understand the possible impact of nanomaterials on human health and the environment. There is to date limited evidence of actual harm resulting from the use of nanomaterials, nevertheless there is a common acceptance that this is a possibility and that there is indeed a need for more research.

The European Commission (EC) already noted in the report *Nanoscience and nanotechnology: An action plan for Europe 2005-2009*[1], that all products based on nanomaterials must comply with the high level of public health, safety, consumer and workers protection, and environmental protection chosen by the Community. In a regulatory review from June 2008[2], addressed to the European Parliament (EP), the EC considers that the management of the possible risks from nanomaterials in relation to health, environment and safety is in principle covered by existing legislation even if nanomaterials are not explicitly mentioned. However, the EC will also consider changes to legislation whenever the need for specific risk management measures becomes apparent.

The EC review was extensively debated within the EP. In its report on regulatory aspects of nanomaterials, of 24 April 2009[3], the EP concluded that 'the current discussion about nanomaterials is characterised by a significant lack of knowledge and information, leading to disagreement and political struggles starting at the level of definitions'. Consequently, the EP called

> 'for the introduction of a comprehensive science-based definition of nanomaterials in Community legislation as part of nano-specific amendments to relevant horizontal and sectoral legislation', and
>
> 'on the Commission to promote the adoption of a harmonised definition of nanomaterials at the international level and to adapt the relevant European legislative framework accordingly'.

With 'science-based' it is here understood that the definition should be based on established scientific principles. The EC presented a positive feedback to the EP resolution.

The introduction of a definition of 'nanomaterial' is, however, not straightforward. No internationally harmonised definition yet exists that would fulfil the requirements for entering into legislation, even though a wide range of definitions have indeed been discussed and proposed by national authorities, scientific committees, international organisations, and others. The multitude of definitions currently available also counteracts the power and strength of each individual definition, since in this way each definition is applicable either only in a very specific sector or within a certain organisation

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[1] ftp://ftp.cordis.europa.eu/pub/nanotechnology/docs/action_plan_brochure.pdf

[2] *Regulatory aspects of nanomaterials*, COM(2008) 366, http://ec.europa.eu/nanotechnology/pdf/comm_2008_0366_en.pdf

[3] European Parliament, *Report on regulatory aspects of nanomaterials*, A6-0255/2009.

and its activities. This is a source of ambiguity and confusion for those directly concerned with regulation and also for the general public.

The aim of this report is to discuss elements of a definition of the term ‘nanomaterial’ based on a scientific analysis of related issues as well as a review of currently available definitions. The report provides a practical approach and guidance for a definition aimed for regulatory use. Since only those materials which are in a particulate form at the nanoscale, and are mobile in their immediate environments, raise health and environmental concerns, it may be advisable, as discussed in Chapter 4, to use the more specific term ‘particulate nanomaterial’ in such a context.

1.1. Properties at the nanoscale

Nanomaterials often display different chemical, physical, and biological characteristics, and thus behave differently, with respect to materials of a coarser structure, even when the elemental or molecular composition is the same. Some of their properties can be extrapolated from the macroscale, whereas others change drastically below a certain size.

Nanomaterials have a much larger specific surface or interface area, i.e. a larger area to mass ratio, than coarser materials. For spherically shaped nanoparticles, the specific surface area increases with the inverse of the diameter. From purely geometrical considerations, as an example, 10 g of silver in the form of spherical nanoparticles with a diameter of 10 nm exhibits a total surface area of almost 600 m^2. This should be compared to a single solid silver sphere with the same mass which has a surface area of nearly 5 cm^2, giving an increase in total surface area for the nanomaterial form of a factor of about 1,200,000. A powder with grains of a diameter of 50 µm (similar to cement powder) would only have a surface area increase of a factor of less than 250 with respect to the single sphere. Since biological and chemical reactions often take place at the surface of materials, one expects nanomaterials to be much more reactive than the same mass of material made up of coarser structures. In addition, as a consequence of their small size, nanoparticles may migrate easier in biological systems like the human body, and be able to cross biological barriers in the lung, gut, or the brain, and therefore cause unexpected and unusual exposure.

Furthermore, there are intrinsic nanoscale properties which result from the confinement of atoms and electrons within boundaries of a few nanometres. These effects are most dominant at sizes below a few tens of nanometres (less than about 30 nm). They can considerably change fundamental physical material characteristics like the optical, electrical, and magnetic properties of the nanomaterial. Comprehensive summaries of material properties at the nanoscale can be found in the literature[4,5,6].

1.2. Nanomaterials available today

Some materials which are regarded as nanomaterials today have already been on the market for a long time. The well known nanomaterial ‘carbon black’ was used in industrial production over a century ago. In 1915 it was introduced as a reinforcing agent for the production of car tyres[7] and today the annual production exceeds 10 million tons, still mostly for car tyres. Other early nanomaterials are fumed silica, a form of silicon dioxide (SiO_2), and later on also titanium dioxide (TiO_2), and zinc oxide (ZnO). These four nanomaterials are still, together with the more recently introduced silver nanoparticles, the most used in terms of commercial production amounts and represent the main volume of what is introduced into consumer products available on the market.

A considerable number of other nanomaterials are available and new nanomaterials are constantly being developed and introduced. In a report from the EC in 2009 on *Nanosciences and Nanotechnologies: An action plan for Europe 2005-2009 - Second Implementation Report 2007-2009*[8] a number of nanomaterials existing on the market, or being used for

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[4] *Springer Handbook of Nanotechnology*, Bhushan, Bharat (Ed.), 2nd rev. and extended ed., 2007.

[5] http://www.ea-aw.de/fileadmin/downloads/Graue_Reihe/GR_35_Nanotechnology_112003.pdf
Schmid, G. et.al., *Small Dimensions and Material Properties A Definition of Nanotechnology*, November 2003.

[6] Auffan, M. et al., ‘Towards a definition of inorganic nanoparticles from an environmental, health and safety perspective’, *Nature nanotechnology*, vol.4, October 2009, 634-641.

[7] The Handbook of Texas – On-line, http://www.tshaonline.org/handbook/online/articles/CC/doc1.html

[8] *Nanosciences and Nanotechnologies: An action plan for Europe 2005-2009 - Second Implementation Report 2007-2009*, http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=SEC:2009:1468:FIN:EN:PDF

research and development purposes, are reported, see Table 1. Some of these are, however, used only in very few special cases and it is not clear whether several are available at all on the European market. Most of the materials in Table 1, e.g. silver, iron, aluminium oxide, cerium oxide and polystyrene, are in the form of nanoparticles, whereas some also exist in the form of nanotubes and nanorods. Carbon is also available in the form of fullerenes which are molecules composed entirely of carbon (for example C_{60}). Nanoclay is clay from the smectite family having a unique layered morphology with layer spacing in the nanometre range.

1.3. Applications of nanomaterials

By using nanomaterials, every-day consumer products may be made lighter, stronger, cleaner, less expensive, more efficient, more precise, or more aesthetic. Products containing nanomaterials may improve our quality of life through more efficient target driven pharmaceuticals, better medical diagnosis tools, faster computers, cleaner energy production, etc. Several of the consumer end-products available today that utilise nanomaterials have been developed from existing products, for example by the incorporation of nanomaterials into solid, viscous or liquid matrices.

Examples of product areas with end-products containing nanomaterials are:

- cosmetics and personal care products
- paints & coatings
- household products
- catalysts & lubricants
- sports products
- textiles
- medical & healthcare products
- food and nutritional ingredients
- food packaging
- agrochemicals
- veterinary medicines
- construction materials
- weapons & explosives
- consumer electronics.

About one third of the products are sunscreen lotions or cosmetics such as skin-care and colorant products[9]. For sunscreens, titanium dioxide and zinc oxide nanoparticles are used as they absorb and reflect ultraviolet rays but are still transparent to visible light and, thus, the resulting sunscreen becomes both more appealing to the consumer and is claimed to be more effective. Also liposomes, i.e. tiny vesicles made out of the same material as cell membranes, are known to be used in

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[9] The Woodrow Wilson Nanotechnology Consumer Products Inventory, http://www.nanotechproject.org/inventories/consumer/

Table 1. Non exhaustive list of nanomaterials either currently used commercially or being produced in significant quantities for research or development purposes.

Aluminium
Aluminium Oxide
Aluminium Hydroxide
Antimony Oxide
Antimony Pentoxide
Barium Carbonate
Bismuth Oxide
Boron Oxide
Calcium Oxide
Carbon Black
Cerium Oxide
Chromium Oxide
Cluster Diamonds
Cobalt
Cobalt Oxide
Colloidal Gold
Copper (II) Oxide
Dendrimers
Dimethyl Siloxide
Dysprosium Oxide
Fullerenes
Germanium Oxide
Indium Oxide
Iron
Iron Oxides
Lanthanum Oxide
Lithium Titanate
Manganese Oxide
Molybdenum Oxide
Nanoclays
Neodymium Oxide
Nickel
Niobium
Palladium
Platinum
Polyethylene
Polystyrene
Praseodymium Oxide
Rhodium
Samarium Oxide
Silanamine
Silicon Dioxide
Silver
Single- and Multi-walled nanotubes
Tantalum
Terbium Oxide
Titanium Dioxide
Tungsten
Yttrium Oxide
Zinc Oxide
Zirconium Oxide

the cosmetics industry. In fact, there are very many cosmetic products that have nanomaterial content and the frequent use of nanoparticles in cosmetics has indeed raised a number of concerns about consumer safety, since they are applied directly on the human body.

More advanced innovations are being developed and introduced on the market at an increasing pace. The *NanoRoadSME's Nanomaterial Roadmap 2015*[10] (2005) lists a large variety of promising nanomaterials with high potential for future industrial applications in different sectors. These, and others, where nanotechnology has or is foreseen to have a considerable impact, include:

- medical and pharmaceutical sector
- bio-nanotechnology, bio-sensors
- energy sector, including fuel cells, batteries and photovoltaics
- environment sector including water remediation
- automotive sector
- aeronautics sector
- construction sector, including reinforcement of materials
- composite materials
- electronics and optoelectronics, photonics.

It should be noted, however, that composite materials and electronics are not always considered as products derived from nanotechnology, or as utilising nanomaterials, even if nanoscale materials and structures are included. Several composite materials, such as the rubber used in car tyres have, as mentioned above, been available for a long time and have never been considered as a special technology due to the nanomaterial ingredients. Electronic devices are often considered as being more a result of miniaturisation than as based on a novel (nano)technology, even if devices with structures smaller than 100 nm are today routinely manufactured and used in memory chips, high speed electronics and other integrated devices. However, future electronic devices may very well incorporate and deliberately exploit specific nanoscale properties, for applications such as single electron devices, e.g. single electron transistors or quantum cells.

Materials with typical external dimensions or internal features in the nanometre range may have novel properties not observed for coarser structures. They are more and more used in highly innovative products, which enter the market at a steady rate. However, the potential impact of these new materials on human health and the environment is not well known. This raises concerns about possible risks associated with the handling and use of such materials.

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[10] http://www.nanoroad.net/download/overview_nanomaterials.pdf

2. The need for a definition of the term 'nanomaterial'

Definitions help to avoid misunderstandings and to ensure efficient communication. For regulatory purposes, a definition should be as clear and simple as possible, but at the same time unambiguous and comprehensive. Considering the term 'nanomaterial', there is neither a global nor an agreed EU definition yet available, although what are understood as being nanomaterials are already manufactured, commercialised and used, as outlined in the introduction. Thus, representatives from science, industry and regulatory bodies concerned with subjects of nanotechnology, currently lack, and strongly need, a common definition for the term 'nanomaterial'. This need is also acknowledged by the European Parliament, which asked the European Commission for the introduction of a comprehensive science-based definition of the term 'nanomaterial' in Community legislation, a definition that could very well affect a significant number of EU regulations and directives.

With respect to relevant EU legislation, one can distinguish between horizontal legislation (e.g. chemicals legislation, worker protection and environmental legislation) and sector specific legislation (e.g. cosmetic products, food legislation, biocidal products, plant protection products, medicinal products and devices, aerosol dispensers, electronic industry, automotive industry, etc.). Current EU legislation applies to nanomaterials without specifically addressing them, with the exception of recently discussed or adopted legislation (see below). The question is whether this is satisfactory or whether there is a need for modification to current legislation in order to ensure appropriate hazard identification and/or consumer information.

The most comprehensive horizontal piece of legislation in this context is probably the EU chemicals legislation, REACH (Registration, Evaluation, Authorisation and Restriction of Chemicals)[11]. REACH applies to chemical 'substances' on their own, in mixtures or in articles:

> 'Substance means a chemical element and its compounds in the natural state or obtained by any manufacturing process, including any additive necessary to preserve its stability and any impurity deriving from the process used, but excluding any solvent which may be separated without affecting the stability of the substance or changing its composition.'12

Thus, the substance definition in REACH goes beyond a pure chemical compound described by a single molecular structure and includes different constituents such as impurities and additives necessary to preserve its stability. There are no provisions in REACH referring specifically to nanomaterials, but REACH addresses chemical substances, in whatever size, shape or physical state (CA/59/2008 rev.1)[13]. Substances at the nanoscale are therefore covered by REACH and its provisions apply. The same applies to other legal instruments which use the same (Biocidal Products Directive[14] and Cosmetic Products Regulation[15]) or a similar (Plant Protection Products Directive[16]) substance definition as REACH.

The new Cosmetic Products Regulation includes a labelling obligation for ingredients present in the form of nanomaterials, i.e. in the list of ingredients the names of such substances shall be followed by the word 'nano' in brackets. This is not meant to be a hazard labelling, but is only for information and will allow consumers to make a choice. Nevertheless, it requires the adoption of a definition. Thus, the Cosmetic Products Regulation introduces the definition:

> '"nanomaterial" means an insoluble or biopersistant and intentionally manufactured material with one or more external dimensions, or an internal structure, on the scale from 1 to 100 nm'

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[11] Regulation (EC) No 1907/2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals. – OJ L 136, 29.5.2007, p. 3.

[12] Article 3 of the REACH Regulation (EC) No 1907/2006.

[13] Nanomaterials in REACH (CA/59/2008 rev.1): http://ec.europa.eu/environment/chemicals/reach/reach_intro.htm or http://ec.europa.eu/enterprise/sectors/chemicals/reach/nanomaterials/index_en.htm

[14] Directive 98/8/EC concerning the placing of biocidal products on the market. -– OJ L 123, 24.4.1998, p. 41.

[15] Regulation (EC) No 1223/2009 on cosmetic products. – OJ L 342, 22.12.2009, p. 59

[16] Directive 91/414/EEC concerning the placing of plant protection products on the market. - OJ L 230, 19.8.1991.

(see also Chapter 3.2.4 of this report). The Regulation also includes a review clause, which states that the definition shall be adapted to technical and scientific progress. Other Regulations/Directives with such provisions might follow, e.g. the Novel Foods Regulation.[17]

This raises the question as to whether a 'harmonised' definition of nanomaterial over and across the different regulatory areas is necessary or even appropriate. The advantage of different definitions would be that the definitions could be tailored to the needs of specific legislative instruments. However, a chemical substance might be used in different industrial sectors and areas of application. Thus, different definitions would lead to the situation, that the same substance could be regarded as a nanomaterial under one legal instrument, but not under another. This would create confusion, not only for the consumer, but also for industry and regulators. Therefore, a single definition would be desirable if it could be made broadly applicable in EU legislation and policies, for example in chemicals legislation, worker protection legislation, and legislation on air and water quality or waste. The implicit condition - even if difficult to achieve - is that such a common definition is suited for all the regulations and policies it intends to serve.

As required for legal instruments, the definition must be clear and unambiguous in order to be easy to implement. In addition, compliance checks must be possible, e.g. in order to assess whether the labelling requirements according to the Cosmetic Products Regulation are fulfilled. Thus, the definition must be enforceable. This implies that appropriate measurement techniques are available and methods and procedures for their application are agreed.

To preserve the integrity of the EU internal market, it is necessary to ensure that a definition is accepted by all EU Member States, thus avoiding claims of additional national regulatory needs. Furthermore, in light of the global market, a European definition should be in line with international initiatives (e.g. OECD and ISO).

Finally, it should be considered that each definition will have implications within the context in which it is used. Therefore, any definition will also involve policy choices, and accordingly it will inevitably entail political decisions.

For regulatory purposes a definition of 'nanomaterial' should ideally fulfil the requirements of being:

- **a single definition broadly applicable in EU legislation and policies,**
- **legally clear and unambiguous,**
- **enforceable through agreed measurement techniques and procedures, and**
- **in line with other approaches worldwide.**

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[17] Commission proposal for a Regulation on novel foods and amending Regulation (EC) No 258/97. – 14.1.2008, COM (2007) 872 final, 2008/0002 (COD)

3. Overview of proposed nanomaterial definitions

Several national and international standardisation bodies, organisations, and authorities have developed a definition for the term 'nanomaterial' and released terminology documents for nanotechnology. Some of these definitions are reviewed below and are summarised in Tables A1–A4 in the Appendix. Many of the released documents so far are non-normative, and some have been published merely in an attempt to collect feedback from stakeholders. Because these efforts have resulted in a number of partially conflicting definitions, there is a general consensus that further development of nanotechnology terminology documents should no longer be pursued on a national or regional basis, but rather at a European or global level.

3.1. Definitions regarding nanomaterials by the International Organisation for Standardisation (ISO) and the European Standardisation Committee (CEN)

Technical Committee (TC) 229 of the International Organisation for Standardisation (ISO) is the main TC responsible for standardisation work related to nanotechnologies. In addition to a number of specific working groups, ISO/TC 229 has established a Nanotechnologies Liaison Coordination Group to further harmonise the work of relevant ISO technical committees as well as other organisations, and to identify gaps and cross cutting opportunities.

Within the European Standardisation Committee (CEN), Technical Committee (TC) 352 deals with nanotechnologies. Many of the members of CEN/TC 352 also participate in ISO/TC 229, and consensus has been achieved in CEN/TC 352 not to initiate or lead projects concerning terminology issues, but rather to support the nanotechnology terminology efforts of the ISO/TC 229/JWG 1 Terminology and Nomenclature, which is a joint working group between ISO and IEC, the International Electrotechnical Commission. There is an agreement within CEN/TC 352 to systematically propose the ISO/IEC documents, related to terminology for nanotechnologies, for adoption as CEN documents using the Vienna Agreement process[18]. A number of nano-related definitions have already been published by ISO in Technical Specifications (TS), which can be freely consulted via the on-line ISO Concept Database[19].

The terminology work related to nanomaterials in ISO is divided into different sub-activities:

- ISO/TC 229/JWG 1 has finalised and released the technical specification (TS) *CEN ISO TS 27687 Nanotechnologies — Terminology and definitions for nano-objects — nanoparticle, nanofibre and nanoplate* in 2008. After revision, it will be released with a new number, ISO TS 80004-2.

- In the same series (80004 nanotechnology-related terminology documents) a second document has recently been published: *ISO/TS 80004-3: 2010 Nanotechnologies — Vocabulary — Part 3: Carbon nano-objects*. This document defines terms such as graphene, fullerene, and carbon nanotube (single-wall and multi-wall).

- The above publications will be followed by the publication of *ISO/TS 80004-1 Nanotechnologies — Vocabulary — Part 1: Core Terms*, which has been approved and is currently being prepared for publication. This document will list a number of core terms, several of which are related to nanomaterials (i.e. nanoscale, nanotechnology, nanoscience, nanomaterial, nano-object, nanostructure, nanostructured material, manufactured nanomaterial, engineered nanomaterial, incidental nanomaterial, nanomanufacturing, nanomanufacturing process, nanoscale phenomenon, nanoscale property).

- Currently, a document defining the main categories of nanostructured material, such as nanostructured powder, nanodispersion, nanolayer, nanocomposite and nanoporous material, is being drafted *(TS 80004-5 Terminology and definitions for nanostructured materials*).

In ISO TS 80004-1 the term nanomaterial is proposed to be defined as:

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[18] http://www.iso.org/iso/about/the_iso_story/iso_story_vienna_agreement.htm

[19] http://cdb.iso.org/ (login as 'guest')

Nanomaterial:	Material with any external dimension in the nanoscale or having internal structure or surface structure in the nanoscale.
Note:	This generic term is inclusive of nano-object and nanostructured material.

The definitions of the terms nano-object and nanoscale are given below. Thus, nanomaterial is here defined as the sum of two subcategories: nano-objects and nanostructured materials. Note that the two categories are partly overlapping: nano-objects can be nanostructured.

The following core terms related to the definition of nanomaterial were released in August 2008 by ISO/TC 229 and by CEN through CEN ISO/TS 27687[19]:

Nanoscale:	Size range from approximately 1 nm to 100 nm[20].
Note 1:	Properties that are not extrapolations from a larger size will typically, but not exclusively, be exhibited in this size range. For such properties the size limits are considered approximate.
Note 2:	The lower limit in this definition (approximately 1 nm) is introduced to avoid single and small groups of atoms from being designated as nano-objects or elements of nanostructures, which might be implied by the absence of a lower limit.
Nano-object:	Material with one, two or three external dimensions in the nanoscale.
Note:	Generic term for all discrete nanoscale objects.

CEN ISO/TS 27687 also quotes an existing general definition for particles from ISO 14644-6:2007, which it specifically applies to nano-objects:

Particle:	Minute piece of matter with defined physical boundaries.
Note 1:	A physical boundary can also be described as an interface.
Note 2:	A particle can move as a unit.
Note 3:	This general particle definition applies to nano-objects.

It is interesting to note that this definition of a particle also includes liquids, e.g. droplets or micelles in emulsions.

CEN ISO/TS 27687 also gives definitions for particles clustered in agglomerates and aggregates. These definitions were prepared in collaboration with ISO/TC 24/SC 4 - Particle characterisation:

Agglomerates:	Collection of weakly bound particles or aggregates or mixtures of the two where the resulting external surface area is similar to the sum of the surface areas of the individual components.
Aggregates:	Particle comprising strongly bonded or fused particles where the resulting external surface area may be significantly smaller than the sum of calculated surface areas of the individual components.

The notes state that agglomerates are weakly bonded, for example by van der Waals forces or simple entanglement, whereas aggregates are held together by strong forces, for example covalent bonds, or those resulting from sintering or complex entanglement. The ISO definition also names agglomerates and aggregates 'secondary' particles to distinguish them from the original individual particles, named 'primary' particles.

CEN ISO/TS 27687 also defines the terminology for some types of nano-objects, including six distinct shapes and an additional specific case (the quantum dot):

Nanoparticle:	Nano-object with all three external dimensions in the nanoscale.
Nanoplate:	Nano-object with one external dimension in the nanoscale and the two other external dimensions significantly larger.
Nanofibre:	Nano-object with two similar external dimensions in the nanoscale and the third dimension significantly larger.
Nanotube:	Hollow nanofibre.
Nanorod:	Solid nanofibre.
Nanowire:	Electrically conducting or semi-conducting nanofibre.
Quantum dot:	Crystalline nanoparticle that exhibits its size-dependent properties due to quantum confinement effects on the electronic states.

[20] While not being explicitly noted in the ISO definition, it is assumed herein that the term 'approximate' refers to both the 1 nm and the 100 nm limits.

3.2. Definitions regarding nanomaterials by other international organisations and committees

3.2.1. Organisation for Economic Co-operation and Development (OECD)

In 2006 the OECD established the Working Party on Manufactured Nanomaterials (WPMN) under the OECD Joint Chemicals Programme. The WPMN adopted a draft definition given by ISO/TC 229 as an internal working definition for the term 'manufactured nanomaterial'. This working definition has since been applied by the WPMN, while awaiting the release of formally agreed ISO definitions.

The WPMN working definitions, agreed upon at the second meeting in 2007, are:

Nanoscale:	Size range typically between 1 nm and 100 nm.
Nanomaterial:	Material which is either a nano-object or is nanostructured.
Nano-object:	Material confined in one, two, or three dimensions at the nanoscale.
Nanostructured:	Having an internal or surface structure at the nanoscale.
Manufactured nanomaterials:	Nanomaterials intentionally produced to have specific properties or specific composition.
Note 1:	The WPMN considers that fullerene molecules are included within the scope of manufactured nanomaterials.
Note 2:	The WPMN considers that aggregates and agglomerates are nanostructured materials along the lines of ISO.
Note 3:	Those end-products containing nanomaterials (e.g. tyres, electronic equipment, coated DVDs) are not themselves nanomaterials.

3.2.2. EU Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR)

The EU Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR) is one of the independent scientific committees managed by the European Commission (EC), which provides scientific advice to the EC on issues related to consumer safety, public health and environment. In a 2007 Opinion document SCENIHR has, based on an analysis of existing definitions, provided the following suggestions for definitions[21]:

Nanoscale:	A feature characterised by dimensions of the order of 100 nm or less.
Nanostructure:	Any structure that is composed of discrete functional parts, either internally or at the surface, many of which have one or more dimensions of the order of 100 nm or less.
Nanomaterial:	Any form of a material that is composed of discrete functional parts, many of which have one or more dimensions of the order of 100 nm or less.
Nanoparticle:	A discrete entity which has three dimensions of the order of 100 nm or less.
Nanosheet:	A discrete entity which has one dimension of the order of 100 nm or less and two long dimensions.
Nanorod:	A discrete entity which has two dimensions that are of the order of 100 nm or less, and one long dimension.
Nanotube:	A discrete hollow entity which has two dimensions of the order of 100 nm or less and one long dimension.
Nanoparticulate Matter:	A substance comprising of particles, the substantial majority of which have three dimensions of the order of 100 nm or less.

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[21] http://ec.europa.eu/health/ph_risk/committees/04_scenihr/docs/scenihr_o_012.pdf

In an earlier Opinion document of 2006[22], SCENIHR stated

> '… there are two types of nanostructure to consider, those where the structure itself is a free particle and those where the nanostructure is an integral feature of a larger object.
>
> In the latter group are nanocomposites, which are solid materials in which one or more dispersed phases are present as nanoscale particles, and nanocrystalline solids, in which individual crystals are of nanoscale dimensions. This group also includes objects which have been provided with a surface topography with features of nanoscale size, and functional components that have critical features of nanometre dimension, primarily including electronic components…'

and

> 'It is the former group, involving free nanoparticles, that provides the greater concern with respect to health risks, and which is the subject of the major part of this Opinion'.

3.2.3. EU Scientific Committee on Consumer Products (SCCP)

The EU Scientific Committee on Consumer Products (SCCP) issued in December 2007 an opinion on *Safety of Nanomaterials in Cosmetic Products*[23]. The opinion included a glossary of terms 'in the absence of internationally agreed definitions', derived from an earlier report of the British Standards Institution (BSI) of 2005. These included:

Nanoscale:	Having one or more dimensions of the order of 100 nm or less.
Nanoparticle:	Particle with one or more dimensions at the nanoscale.
Nanomaterial:	Material with one or more external dimensions, or an internal structure, on the nanoscale, which could exhibit novel characteristics compared to the same material without nanoscale features.

3.2.4. European Union: Cosmetic Products Regulation

The recent European Cosmetic Products Regulation[15] includes the obligation to label nanomaterials in the list of ingredients. The regulation (Article 2) also provides a definition of a nanomaterial:

Nanomaterial:	An insoluble or biopersistant and intentionally manufactured material with one or more external dimensions, or an internal structure, on the scale from 1 to 100 nm.

It is mentioned in the regulation that the definition shall be adapted to technical and scientific progress.

3.2.5. European Union: Recast of the Novel Foods Regulation

A proposal for a regulation on novel foods (amending Regulation (EC) No 258/97)[17] is currently under discussion. The European Parliament proposes to include a definition of an engineered nanomaterial as meaning:

Engineered nanomaterial:	Any intentionally produced material that has one or more dimensions of the order of 100 nm or less or is composed of discrete functional parts, either internally or at the surface, many of which have one or more dimensions of the order of 100 nm or less, including structures, agglomerates or aggregates, which may have a size above the order of 100 nm but retain properties that are characteristic to the nanoscale.

It is mentioned in the proposal that this definition shall be adjusted once definitions are agreed upon at international level.

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[22] http://ec.europa.eu/health/ph_risk/committees/04_scenihr/docs/scenihr_o_003b.pdf

[23] http://ec.europa.eu/health/ph_risk/committees/04_sccp/docs/sccp_o_123.pdf

3.2.6. American Chemistry Council

The American Chemistry Council (ACC), representing leading companies in the business of chemistry, gives the following definition in the Area of Nanotechnology[24]:

> An Engineered Nanomaterial is any intentionally produced material that has a size in 1, 2, or 3-dimensions of typically between 1-100 nanometres. It is noted that neither 1 nm nor 100 nm is a 'bright line' and data available for materials outside of this range may be valuable. Buckyballs are also included even though they have a size < 1 nm.

The ACC also specifies the following 'inclusion':

> Aggregates and agglomerates with size >100 nm are included if breakdown may occur creating particles in the 1-100 nm range during the lifecycle.

However, the following are specifically excluded as 'engineered nanomaterials':

1. Materials that do not have properties that are novel/unique/new compared to the non nanoscale form of a material of the same composition.
2. Materials that are soluble in water or in biologically relevant solvents. Solubility occurs when the material is surrounded by solvent at the molecular level. The rate of dissolution is sufficiently fast that size is not a factor in determining a toxicological endpoint.
3. For those particles that have a particle distribution such that exceeds the 1-100 nm range (e.g. 50-500 nm) if less than 10% of the distribution falls between 1-100 nm it may be considered as non an Engineered Nanomaterial. The 10% level may be on a mass or surface area basis, whichever is more inclusive.
4. Micelles and single polymer molecules.

It is interesting to note that the text includes instructions on how to deal with the inevitable size distribution of particulate nanomaterials.

3.3. National definitions of nanomaterials

National authorities and organisations on different levels have also provided definitions of the term 'nanomaterial'. The following short overview highlights approaches in some countries.

3.3.1. Australia

The National Industrial Chemicals Notification and Assessment Scheme (NICNAS)[25] concludes in its Chemical Gazette from February 2009[26] that there is currently no agreed national or international definition of nanomaterials. For the purposes of an interim position they use the following working definition:

> '…industrial nanomaterials are those industrial materials intentionally produced, manufactured or engineered to have specific properties or specific composition, and one or more dimensions typically between 1 nm and 100 nm. This size range refers to individual particle size, and does not take into account agglomeration of particles'.

3.3.2. Canada

In an interim policy statement, Health Canada provides a working definition for nanomaterials[27]:

'Health Canada considers any manufactured product, material, substance, ingredient, device, system or structure to be nanomaterial if:

a. It is at or within the nanoscale in at least one spatial dimension, or;

b. It is smaller or larger than the nanoscale in all spatial dimensions and exhibits one or more nanoscale phenomena.

For the purposes of this definition:

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[24] http://www.americanchemistry.com/s_acc/bin.asp?CID=654&DID=5090&DOC=FILE.PDF

[25] http://www.nicnas.gov.au/

[26] http://www.nicnas.gov.au/Publications/Chemical_Gazette/pdf/2009feb_whole.pdf (page 12).

[27] http://www.hc-sc.gc.ca/sr-sr/alt_formats/pdf/consult/_2010/nanomater/draft-ebauche-eng.pdf

> 1. The term “nanoscale” means 1 to 100 nanometres, inclusive;
>
> 2. The term “nanoscale phenomena” means properties of the product, material, substance, ingredient, device, system or structure which are attributable to its size and distinguishable from the chemical or physical properties of individual atoms, individual molecules and bulk material; and,
>
> 3. The term “manufactured” includes engineering processes and control of matter and processes at the nanoscale’.

3.3.3. Denmark

The Danish Ministry of the Environment defines ‘nanomaterials’ in the following way[28]:

> ‘Nanomaterials can be defined as materials which are less than 100 nanometres in length along the shortest side or have structures which have such small dimensions but are build into larger materials (i.e. nanostructured surfaces). A nanometre is a millionth of a millimetre. Nanomaterials can be produced from existing chemical substances or completely new chemical compounds, and can be made from one or more substances. The small size of the materials is reason for their special characteristics.’

3.3.4. The United Kingdom

In 2004 the Royal Society & The Royal Academy of Engineering[29] in the UK published the report *Nanoscience and nanotechnologies: opportunities and uncertainties*. In the report the following definition for ‘nanomaterials’ is given:

> ‘Although a broad definition, we categorise nanomaterials as those which have structured components with at least one dimension less than 100 nm. Materials that have one dimension in the nanoscale (and are extended in the other two dimensions) are layers, such as a thin films or surface coatings. Some of the features on computer chips come in this category. Materials that are nanoscale in two dimensions (and extended in one dimension) include nanowires and nanotubes. Materials that are nanoscale in three dimensions are particles, for example precipitates, colloids and quantum dots (tiny particles of semiconductor materials). Nanocrystalline materials, made up of nanometre-sized grains, also fall into this category’.

The report was followed up by an action in the UK, from 2006 to 2008, to establish a voluntary reporting scheme for engineered nano-scale materials[30] which was organised by the Department for Environment, Food and Rural Affairs, DEFRA[31]. In the guidelines from DEFRA a definition is given as:

> ‘Nano-scale materials are defined as having two or more dimensions up to 200 nm.’

It is stated that the definition will be reviewed according to the ongoing work of BSI, CEN and ISO. The guidelines go on to specify that ‘the focus of the scheme is materials that:

- are deliberately engineered (i.e. not natural or unintentional by-products of other processes)
- have two or more dimensions broadly in the nanoscale; and
- are “free” within any environmental media at any stage in a product’s life-cycle.’

3.3.5. The United States of America

Also in the USA there exists no official definition for ‘nanomaterial’. In the *Concept Paper for the Nanoscale Materials Stewardship Program under TSCA*[32], the US-Environment Protection Agency (EPA) outlines its initial thinking on the design and development of a Stewardship Program for nanoscale materials under the Toxic Substances Control Act

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[28] http://www.mst.dk/English/Chemicals/Substances_and_materials/Nanomaterials/

[29] The Royal Society & The Royal Academy of Engineering, *Nanoscience and nanotechnologies: opportunities and uncertainties*, Latimer Trend Ltd, Plymouth, July 2004 UK, ISBN 0 85403 604 0

[30] http://www.defra.gov.uk/environment/quality/nanotech/documents/vrs-nanoscale.pdf

[31] www.defra.gov.uk

[32] http://www.epa.gov/oppt/nano/nmsp-conceptpaper.pdf

(TSCA). In the paper the term 'engineered nanoscale material' is defined as follows:

> '"engineered nanoscale material" is any particle, substance, or material that has been engineered to have one or more dimensions in the nanoscale.'
>
> 'The term "engineered" is intended to mean that the material is 1) purposefully produced and 2) purposefully designed to be a nanoscale material...'
>
> 'The term "nanoscale" is generally used to refer to the scale measured in nanometres (1 x 10^{-9} meters). For the purposes of the Program, nanoscale is the size range between the atomic/molecular state and the bulk/macro state. This is generally, but not exclusively, below 100 nm and above 1 nm...'.

However, the paper also states that:

> 'The description given herein should not be considered to be definitive for any purpose other than for EPA's Nanoscale Materials Stewardship Program; this definition is only applicable within the context of the Program as a guideline for determining if a material is appropriate for inclusion in the Program.'

3.4. Related definitions in the broader area of Nanotechnology

3.4.1. Definition of nanotechnology

While a definition of the term 'nanomaterial' has been intensively debated during the last years, less focus has been put on a definition of 'nanotechnology'. This is expected since a definition of nanotechnology is of practical use only occasionally, for example when evaluating whether project applications in a 'nano' specific area can be regarded as nanotechnology or not, or when making estimates of the importance of the 'nanotechnology' market. Some also believe that the term 'nanotechnology' will sooner or later cease to exist as researchers and developers study and use materials due to their functionality rather than their size. Nevertheless, a brief comparison of definitions is justified since those for 'nanotechnology' also frequently include a size scale. Whereas the 'nanotechnology' and the 'nanomaterial' size ranges need not necessarily be identical, this was indeed the explicit intention of the ISO in the following definition:

ISO/TC 229

In the ISO/TC 229 the term nanotechnology is (ISO/DTS 80004-1) proposed to be defined as:

> 'the application of scientific knowledge to manipulate and control matter in the nanoscale to make use of size- and structure-dependent properties and phenomena distinct from those associated with individual atoms or molecules or with bulk materials.
>
> Note: Manipulate and control includes material synthesis.'

The 'nanoscale' referred to here is, thus, the same as given in Chapter 3.1.

European Academy, Germany

In a study on a definition of nanotechnology from 2003 by the Europäische Akademie[33] it is proposed not to include any size boundaries at all in the definition of 'nanotechnology' because 'this would imply exclusion criteria independent from the scientific evaluation of the fundamental working principle of a functioning system'. Instead the following definition is proposed:

> 'Nanotechnology is dealing with functional systems based on the use of sub-units with specific size-dependent properties of the individual sub-units or of a system of those'.

Thus, nanotechnology is defined from the functionality aspect only.

European Patent Office

The European Patent Office (EPO) has recently introduced a tagging system for all nanotechnology patent documents. The EPO assigns a 'Y01N' tag to all patent documents containing nanotechnology, where 'Y' is a 'general tagging of new technological developments', '01' tags 'broad technical fields characterised by dimensional aspects' and 'N' indicates nanotechnology which is specified as:

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[33] http://www.ea-aw.de/fileadmin/downloads/Graue_Reihe/GR_35_Nanotechnology_112003.pdf

> 'The term nanotechnology covers entities with a controlled geometrical size of at least one functional component below 100 nm in one or more dimensions susceptible of making physical, chemical or biological effects available which are intrinsic to that size'.[34]

OECD Working Party on Nanotechnology

The OECD Working Party on Nanotechnology (WPN)[35] was established in 2007 with the aim to 'advise upon emerging policy issues of science, technology and innovation related to the responsible development of nanotechnology'. Nanotechnology is by the WPN defined as

> 'the set of technologies that enables the manipulation, study or exploitation of very small (typically less than 100 nanometres) structures and systems. Nanotechnology contributes to novel materials, devices and products that have qualitatively different properties'.

Again, the definition does not include any lower size limit but targets instead nanotechnology products and their properties.

EU Scientific Committee on Emerging and Newly Identified Health Risks

In the Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR) opinion *The scientific aspects of the existing and proposed definitions relating to products of nanoscience and nanotechnologies*[21] of 2007, the term 'nanotechnology' is not specifically defined. However, the following statement is made:

> 'It is widely accepted that although the prefix nano specifically refers to 10^{-9} units, in the context of nanoscience the units should only be those of dimensions, rather than of any other unit of scientific measurement, such as for time, energy or power.'

Thus, for example, to generate and use pulsed ion beams with nano-second resolution should not be considered as nanotechnology. This might appear obvious for the initiated reader but is an important point to note regarding the development of definitions and terminology.

American National Standards Institute - Nanotechnology Standards Panel

The American National Standards Institute's Nanotechnology Standards Panel (ANSI-NSP)[36] serves as the cross-sector coordinating body for the purposes of facilitating the development of standards in the area of nanotechnology, including nomenclature and terminology, materials properties and testing, and measurement and characterisation procedures. The panel adopted a definition for 'nanotechnology' from the National Nanotechnology Initiative (www.nano.gov) as:

> '...the understanding and control of matter at dimensions of roughly 1 to 100 nanometres (one-billionth of a meter), where unique phenomena enable novel applications. Encompassing nanoscale science, engineering and technology, nanotechnology involves imaging, measuring, modelling, and manipulating matter at this length scale'.

ASTM International

ASTM International is an international standards organisation that developed from the American Society for Testing and Materials (ASTM). ASTM International publishes voluntary consensus technical standards for a wide range of materials, products, systems, and services. In an attempt to set a standard terminology relating to nanotechnology (ASTM E2456-06), a precautionary remark is made, including what can also be considered as a choice of the size range of nanomaterials[37]:

> 'As nanotechnology is a rapidly developing field, it will be necessary to continually reassess the terms and definitions contained in this standard, for purposes of revision when necessary. The intent of the terms and definitions in this standard is to describe materials containing features between approximately 1 and 100 nm and to differentiate those properties different from properties found in either molecules or the bulk (interior) of larger, micron-sized systems.'

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[34] http://documents.epo.org/projects/babylon/eponet.nsf/0/623ecbb1a0fc13e1c12575ad0035efe6/$file/nanotech_brochure_en.pdf

[35] http://www.oecd.org/site/0,3407,en_21571361_41212117_1_1_1_1_1,00.html

[36] http://www.ansi.org/nsp/

[37] ASTM E2456 - 06 Standard terminology Relating to Nanotechnology

3.4.2. Definitions of aerosols

An aerosol is a multi-phase system of liquid or solid particles suspended in air or another gas mixture. The size spectrum of aerosol particles in the atmosphere ranges from a few nanometres to hundreds of micrometres, and thus also includes the nanoscale region. The aerosol size spectrum is traditionally divided into four size 'modes' based on studies of the origin, transformation and deposition of the particles. The nucleation mode encompasses diameters of a few nm. The Aitken nuclei mode is around 40 nm, the accumulation mode around 200 nm, and the coarse mode around 2,000 nm.

Most of the global total aerosol mass is probably found in the coarse mode while the number concentration is certainly dominated by particles of the two smaller modes. On average, about 80% of the aerosol particles are smaller than 100 nm. Typical concentrations range from a few hundred particles per cm^3 in remote areas to millions of particles per cm^3 in highly polluted hot spots, while typical domestic concentrations are about a few thousand per cm^3. Coarse particles are mainly from natural sources such as desert dust suspension and sea spray formation. Natural sources like volcanoes and biogenic emissions of reactive gases followed by the nucleation of condensable photochemical products also produce nanoparticles. However, in inhabited areas, most atmospheric particles and aerosol mass come from human activities, mainly combustion processes (fossil fuel and biomass burning).

For epidemiology studies and regulatory purposes, a second classification scheme is often used which categorises particles according to their equivalent diameter as: ultrafine particles < 100 nm; fine particles < 2,500 nm; coarse particles between 2,500 and 10,000 nm. There is a subtle difference between the ISO definitions for nanoparticles, which are defined based on their geometric size, and ultrafine particles, which are defined based on an equivalent aerodynamic diameter. However, disregarding this difference, most ultrafine particles belong to the nanoscale as discussed previously. Ultrafine particles are distinguished because of their potential specific health risk. PM_{10} and $PM_{2.5}$ (particulate matter with an equivalent aerodynamic diameter smaller than 10 and 2.5 micrometers, respectively) correspond to the inhalable and respirable air-suspended particulate matter fractions, respectively.

3.4.3. Definitions of colloids

A colloid is a system in which particles, which are approximately 1 nm to 1,000 nm in size, are dispersed within a continuous medium. However, the size range in different definitions is not consistent, and varies with the application area. This is illustrated by the following examples:

The *Britannica Concise Encyclopedia*[38] defines a colloid as:

> 'Substance consisting of particles that, although too tiny to be seen with the unaided eye (typically 1 nanometre to 10 micrometres), are substantially larger than atoms and ordinary molecules and that are dispersed in a continuous phase.'

The *Gold Book*[39] of the International Union of Pure and Applied Chemistry (IUPAC) defines 'colloidal' as follows:

> 'The term refers to a state of subdivision, implying that the molecules or polymolecular particles dispersed in a medium have at least in one direction a dimension roughly between 1 nm and 1 µm, or that in a system discontinuities are found at distances of that order.'

The *Oxford Dictionary of Sports Science and Medicine*[40] defines a colloid as:

> 'Small particles (1-100 µm) dispersed in a medium. The particles do not dissolve readily, nor do they settle out under gravity. Colloids have a high capacity for binding with water and other substances. They do not pass easily through cell membranes.'

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[38] *Britannica Concise Encyclopedia*, published by Encyclopædia Britannica, Inc.

[39] IUPAC Gold Book, http://goldbook.iupac.org/index.html

[40] *Oxford Dictionary of Sports Science and Medicine*, ed. Kent, ISBN: 0-19-921089-6, Oxford University Press, 2006

4. Considerations on a definition for regulatory purposes – elements of a definition

As noted above, a comprehensive science-based and harmonized definition of the term 'nanomaterial' is now considered as being crucial for regulatory purposes. In general, regulation requires the definition of the items that should be regulated. Defining the term 'nanomaterial' for regulatory purposes would imply that a nanomaterial requires specific regulation as compared to traditional materials. The current use of the term 'nanomaterial' in science and technology often also comprises macroscopic materials with an internal structure designed at the nanoscale (see Chapter 3). In this respect, many traditional materials with nanoscale design ranging from metallic alloys, including for example, steels with special heat treatments, to composite materials with nanosized components should be considered as nanomaterials. This latter broad class of materials is, however, well covered by current legislation and in most cases does not need further consideration from the regulatory point of view. It appears that only those materials which are in a particulate form at the nanoscale, and which are mobile in their immediate environments, raise health and environmental concerns. Hence, for a definition aimed for regulatory purposes that should denote a class of material which requires specific attention in regulation, the term 'nanomaterial' in its current general understanding may not be appropriate. Instead, the term 'particulate nanomaterial', i.e. only nanomaterial in the form of free particles, is considered as being more suitable and will also be the subject of the following discussion. Macroscopic materials with designed internal structure at the nanoscale may be called 'bulk nanomaterials'. This proposal facilitates the continuing use of the term 'nanomaterial' in legislation, while making it clear that it is a special class of nanomaterial to which the legislation refers. The term 'nanomaterial' as used in this Chapter should be understood as 'particulate nanomaterial' if not otherwise stipulated.

The term 'particulate nanomaterial' is proposed also in view of an existing ISO definition of the term 'particle' (see Chapter 3.1) as a 'minute piece of matter with defined physical boundaries' that can 'move as a unit'. It comprises probably most material types and forms such as solid particles, 'soft' nanomaterials, nanotubes, nanofibres, etc., since the ISO definition for a particle includes all types of shapes. In this way, macroscopically stable nanostructured materials would not fall under the scope of the regulation, while agglomerates or aggregates of particles produced from individual smaller particles would be incorporated, as well as fibres with one dimension greater than the nanoscale upper limit.

From the overview in the previous chapter, a few key elements for a definition can be identified including the meaning of the word material, the specification of the nanoscale, and the nanoscale properties. In this Chapter these key elements are addressed and the problems related to the formulation of a definition are discussed.

Questions addressing the key elements for a definition of the term 'particulate nanomaterial':

- **What is a material (in the context of nanomaterial)?** (see Chapter 4.1)
- **What is the size range, i.e. what is the nanoscale?** (see Chapter 4.2)
- **What properties other than size, which are the consequence of the material being at the nanoscale, should be included?** (see Chapter 4.3)

For the term 'nanoscale' specific problems arise, since the lower end of the scale is very close to the atomic scale and within the size range of large molecules, where the intuitive understanding of generic terms such as 'material' as we know them from daily life may fail or become meaningless. On the other hand the term nanomaterial may be useful to capture the novelty of possible applications due to the physical and chemical properties of such a type of material, and hence to coin a term for a material class of its own. Thus, in order to define a 'nanomaterial', it is necessary to clarify the term 'material' first.

4.1. The term 'material'

The term 'material' is not defined in current legislation and is often used intuitively. A 'material' is what a thing is or what it is made of (*Webster's New World College Dictionary*, 2009[41]), a quantity of matter (*ISO 10303-227:2005*)[42]. Of the 28 ISO documents which currently provide a definition for 'material', most describe it as a 'single basic substance or uniformly dispersed mixture of substances'. 'Material' is here, thus, related to the term 'substance', and indeed 'material' is often used synonymously with the term 'substance'. However, 'substance' is already defined (see Chapter 2) in the REACH Regulation[43], which should also cover nanomaterials, and applies to chemical substances, on their own, in 'mixtures' or in articles.

It is, however, not advisable to use 'material' as a synonym for 'substance' in the context of REACH. There are many examples of (nano)materials that are engineered at the nanoscale, e.g. well-defined coatings, specific surface functionalisations, complex geometrical shapes and functionalities (e.g. hollow spheres as carriers for other substances). Such materials therefore exhibit a well-defined structural organisation and combination of various substances in the nanometre range. Likewise, the term 'mixture' as used in REACH is neither adequate since, for example, coated nanoparticles are not just mixtures but contain a certain degree of order and organisation. Hence, using the terms 'substance' or 'mixture' as applied in REACH would not be adequate.

For the sake of clarity and broad applicability of a definition, it is necessary to avoid both ambiguity and any conflict with existing definitions used for regulatory purposes. For the purpose of defining 'nanomaterial' it is suggested to use the term 'material' to refer to 'a single or closely bound ensemble of substances at least one of which is in a condensed phase, where the constituents of substances are atoms and molecules'. The term 'condensed phase' is generally used in thermodynamics for phases where a strong interaction between the constituents (i.e. atoms and molecules) exists; therefore either the solid or liquid phase of a substance.

The term 'material' is proposed to refer to a single or closely bound ensemble of substances at least one of which is in a condensed phase, where the constituents of substances are atoms and molecules.

Using this concept, inorganic, organic, and various types of 'soft' natural and manufactured nanomaterials, as used for example in cosmetics and possibly in the food sector, such as nanoemulsions, liposomes, micelles and various forms of nanocarriers would be fully included. It also makes use of the term 'substance' which is well defined in REACH. It should also be noted that with this definition, single molecules are not included (e.g. large biomolecules which can reach sizes of several nanometres), an issue which is left open in most of the currently proposed definitions. Here, however, particular attention has to be drawn to fullerenes which are single, carbon-based molecules, for example C_{60}, which are most often regarded as nanomaterials. A similar issue may arise with dendrimers.

4.2. The 'nanoscale'

Practically all definitions currently used by different organisations, at international or national level, include a size range when defining 'nanomaterial'. A size range is needed to distinguish a 'nano'material from materials with external dimensions in the micrometre range or larger, and from the sizes at the atomic and molecular level.

The definition of the term nanoscale as recently given by ISO encompasses the size range from approximately 1 nm to 100 nm, a range which has been adopted in a number of other definitions as well. Note that ISO uses the word 'approximately', which is assumed to be applicable for both the lower and the upper limits of the definition. Size can refer to all three spatial dimensions and can therefore as well be used to characterize coarse shapes, such as spherical, oblate, prolate, fibre-like, or sheet-like. Additionally, some proposed definitions also address internal or surface structures or features, using the same size range.

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[41] *Webster's New World College Dictionary*, IDG Books Worldwide Inc., Micheal Agnes editor in chief, ISBN: 0-02-863119-6 (plain).

[42] *ISO 10303-227:2005, Industrial automation systems and integration -- Product data representation and exchange -- Part 227: Application protocol: Plant spatial configuration.*

[43] Regulation (EC) No 1907/2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals. – OJ L 136, 29.5.2007, p. 3.

4.2.1. Size measurement

For a size-based definition to be enforceable, the availability of techniques for measuring size are crucial. Although the size of an object can be measured from less than 1 nm and upwards, such size measurements are not straightforward. Several techniques are available, but not all are suitable for routine analysis. Different methods, based on different measurement principles, may yield different results when measuring the very same object or structural feature. It is therefore necessary to develop, validate and use standardised and internationally agreed methods and protocols, including for the measurement of the size distribution of particle populations.

For particulate nanomaterials, there exist several methods. However, for materials other than perfectly spherical nanoparticles, the results of these methods are often not comparable. Until the behaviour of nanoparticles during size measurements is better understood, measured particle size values should be regarded as 'method-dependent', and should be reported with an indication of the used analytical technique and the applied protocol[44]. A few examples of methods and the particular issues associated with them are given below. A more comprehensive overview is given by Hasselloev and Kaegi[45].

Single particle methods

If an individual nanoparticle can be isolated and fixed on an appropriate sample holder, it can be precisely visualized and measured by (high-resolution) transmission or scanning electron microscopy, or by scanning probe microscopy. However, the sample preparation is tedious and time-consuming and the measured characteristics do not necessarily fully reflect the original particle. Furthermore, every measurement refers to a single nanoparticle (*single particle method*) and only relatively few nanoparticles are visible simultaneously. Therefore statistical significance is a problem, particularly for poly-disperse samples, in which case there are also difficulties with obtaining a representative sample of particles. These issues can be addressed by measuring multiple samples and using automated image recognition software for size determination, but only at the expense of time and costs.

Ensemble methods

For the sizing of large numbers of nanoparticles, standard methods are available today for the measurement of monodisperse powders in low-viscosity suspensions. However, these methods are not always suitable for the measurement of size distribution of polydisperse particle populations or for a high concentration of particles in a matrix.

Most non-microscopy methods determine the nanoparticle size in an indirect manner, for example by observing light scattering from a large number of particles, and thus refer to an ensemble of particles (*ensemble method*). Such indirect methods often provide other measurands, from which size is calculated by means of a physical model. However, different ensemble methods are likely to give different size values for the very same sample of particles, and the calculated 'equivalent' diameters are not easily compared with the geometric particle sizes measured by means of single particle methods.

In the most favourable case, a particle sizing method is also capable of measuring the size distribution of the particles. However, the most commonly used method for suspended nanoparticles, dynamic light scattering (DLS) operated in accordance with ISO 13321 and ISO 22412, does not provide a full particle size distribution. Instead, the method produces a single average value and a number (the 'polydispersity index') indicating the polydispersity of the particle population. There are indeed software routines that facilitate the calculation of a particle size distribution from DLS data, but the adequacy and the comparability of these routines needs to be further evaluated.

In aerosol physics, the most commonly used methods for particle sizing are differential electrical mobility (from about 10 nm to 1000 nm; ISO 15900:2009) and light scattering aerosol spectrometry (from 60 nm to 45 µm; ISO 21501-1:2009). These two methods allow the determination of the equivalent aerodynamic diameters which may be different from the geometric diameter measured with microscopy techniques.

[44] Lamberty, A., Franks, K. , Braun, A., Kestens, V., Roebben, G., Linsinger, T., *Interlaboratory comparison of methods for the measurement of particle size, effective particle density and zeta potential of silica nanoparticles in an aqueous solution*, IRMM internal report RM-10-003 (2010).

[45] Hasseloev, M., Kaegi, R., 'Analysis and Characterization of Manufactured Nanoparticles in Aquatic Environments', *Environmental and Human Health Impacts of Nanotechnology,* Eds. Jamie R. Lead and Emma Smith, Blackwell Publishing Ltd, 2009.

Size is a property which can be measured from less than 1 nm to the macroscale. There are two principal categories of measurement techniques:

- **Single particle measurement methods**
- **Ensemble methods**

For the comparison of size results obtained with different methods, theoretical assumptions for deriving size values must be carefully taken into account.

4.2.2. Upper size limit

In currently used definitions of nanomaterials (see Chapter 3), but also more generally in the nanotechnology area, an upper limit of 100 nm is frequently used to distinguish the nanoscale from the micro- and macroscale. Sometimes qualifiers like ‘approximately 100 nm’ or ‘of the order of 100 nm’ are also included. The use of a soft upper limit, implicitly assumes that there are some other properties which need to be taken into account when deciding whether some material qualifies as a nanomaterial. In any case, such a softening of the upper size limit can not be considered supportive of a clear definition and may render difficulties for the legal enforceability of a definition.

An upper limit of 100 nm does not capture all types of materials with genuine nanoscale properties that would need particular attention for regulation. Many types of particles with individual diameters below 100 nm tend to aggregate or agglomerate due to attractive forces between the individual particles. The resulting aggregates or agglomerates, can easily become much larger than 100 nm (see Chapter 3.1 for the definitions of aggregate and agglomerate). They may, however, still retain certain properties of the individual nanoparticles, particularly agglomerates which are more loosely bound than aggregates and, hence, exhibit a surface area of the order of the sum of those of the individual particles. Thus, specific nanoscale properties may be found in aggregates and agglomerates, even if the diameters are far beyond 100 nm.

Furthermore, specific types of nanostructures as carriers of substances are now being developed and studied, with applications for example in medical therapy, cosmetics and food. Such ‘nanocarriers’ could, for example, be liposomes or micelles that consist of an organic shell enclosing a central compartment which can be loaded with drugs or other substances. The outer diameter of such carriers can be much larger than 100 nm, while the internal functional features are smaller than 100 nm.

It has to be considered if, and how, these larger particles should be captured by a definition of nanomaterial. Their retained nanoscale properties, which can be very different depending on the type of material (e.g. micelles vs. agglomerates/aggregates of nanoparticles), suggest that they indeed should be included. To accomplish this, three options may be discerned:

1. To keep the upper limit of 100 nm and to introduce in the definition of nanomaterial one or more qualifiers based on structural features (for example as in the ISO definition) and/or functional properties other than size.
2. To keep the upper limit of 100 nm and to particularly mention, in a specifying note, the concerned nanomaterials and nanomaterial formations larger than 100 nm (for example ‘nanomaterials and their aggregates and agglomerates’).
3. To establish an upper limit (e.g., in the range between 100 and 1000 nm) which also encompasses those materials.

In the interest of a single, clear, broad and enforceable definition the third option clearly has some advantages. However, it should be noted that, in a regulatory context, the higher the upper limit chosen, the higher will be the inclusion of materials that do not exhibit specific properties or behaviours due to their nanoscale size.

4.2.3. Lower size limit

Most currently used definitions have established 1 nm as the lower limit of the nanoscale. Sometimes this value, as the upper limit, is given as a soft limit (‘approximately’, ‘of the order of’), and some definitions leave the lower limit open (see Chapter 3).

A lower limit is helpful to distinguish particulate nanomaterials from atoms or molecules which are considered as the constituents of the substances which, in turn, constitute the condensed phases making up a (nano)material. Atoms and molecules are the subject of well established and more traditional areas of research in physics and chemistry. There is little disagreement that single atoms and most molecules – molecule being defined as the simplest structural, electrically neutral unit of an element or compound held together by very strong (covalent) chemical bonds - should not be regarded as nanomaterials. The largest atom, caesium, has a diameter of about 0.6 nm while also most molecules are smaller than 1 nm. Thus, 1 nm appears to be a reasonable value for a lower limit. As sizes of the order of 1 nm can be measured by means of high-resolution transmission electron microscopy, the enforceability of a definition that contains such a lower size limit appears to be feasible. Large biomolecules (e.g. enzymes) may have dimensions well above 1 nm which would, however, be excluded by the concept of 'material' introduced previously since single atoms or molecules do not constitute a condensed phase. Nevertheless, it is advisable to include a lower limit for clarity.

Again, particular attention has to be drawn to fullerenes which may very well have all three dimensions smaller than 1 nm. Nevertheless, fullerenes are, as mentioned above, often regarded as nanomaterials and should be explicitly included.

In order to base a nanomaterials definition for regulatory purposes on size alone, the upper nanoscale limit should ideally be high enough to capture all types of materials that would need particular attention for regulation due to their nanoscale size.

Upper limits which are often used in existing definitions, for example 100 nm, may require the introduction of one or more qualifiers based on structural features or properties other than size, in order to capture structures of concern (for example agglomerates or aggregates) with a size larger than 100 nm in the regulation.

Establishing a nanoscale size range with rigid limits would be advantageous for a clear, single and broad definition and would be important with regards to enforceability of a definition in a regulatory context. For pragmatic reasons, a lower limit of 1 nm and an upper limit of 100 nm or greater is a reasonable choice.

4.2.4. Size distribution

A sample of particles with nanoscale dimensions will not be uniform in size but will inevitably have a size distribution. A sample may thus contain material outside the limits of a size range specified in a definition, even if the mean value is well within the limits. Likewise, samples with a given average size larger than an upper size limit, may very well contain a considerable fraction of particles whose size falls within the range of a nanoscale definition. If a specific size range is to be established for the definition of nanomaterial, it is therefore important to clarify how characteristic values can be extracted from a size distribution, which then can be used to decide whether a material meets the definition of nanomaterial. For instance, when calculating an average value for a nanoparticle population, there are different weighting methods. Some methods give an equal weight to every particle in the population, other methods weight the contribution of a particle to the average size by the volume of the particle, and many methods actually weight the contribution of an individual particle by the intensity of the measurement signal produced by the particle, which often is a non-linear function of the particle size. It should also be noted that, even within a single method, there are multiple ways of determining an average. The average can be an arithmetic average, a harmonic average, a median value, a modal value. Other size qualifiers to extract size equivalent numbers are also possible and it needs to be clarified and agreed upon which value should be applied for a definition.

From this discussion, it follows that the size of nanoparticles in large populations is potentially an ambiguous property if not accurately specified. To be able to compare and correctly understand reported size values it is, as also discussed above, essential that sufficient detail is provided about the method which was used to acquire the data, and about the method which was used to deduce the size from the measured raw data.

A material may also be regarded as 'nano' even though it contains a certain fraction of 'non-nano' material, e.g., a mixture of particles in the nanometre size range with larger particles. This can be done, for instance, by defining a material as 'nano' if it contains a certain fraction of nanoparticles. The fraction can be based on mass, number, specific surface area or another suitable parameter. The practical, metrological challenges of such qualifiers should however not be underestimated[46].

A definition of 'nanomaterial' which is based on size should as well take into account size distributions and non-uniformity of samples.

4.2.5. Size-related properties

In order to avoid the application of a high upper size limit in a definition of 'nanomaterial', an alternative approach is to use a size-related property as an element of the definition. Such a size-related property, for example the specific surface area[47], could be used as one of, or even *the* sole criterion in the definition. However, due to the requirement of enforceability of a definition, the associated method of measurement must be very carefully standardised and guarantee reproducibility. For the measurement of specific surface area, a standard method is indeed available for dry powders.[48] On the other hand, no generally applicable method exists for the measurement of the surface area of particles suspended in liquids. It appears today to be more problematic to exclusively use such a size-related property, instead of the size itself, as the defining element. This should, however, not be confused with definitions related to the exposure to nanomaterials ('dose') where specific surface area very well may turn out to be an appropriate measurand.

It is preferable to use the size itself in a definition of 'nanomaterial', instead of properties which are directly or indirectly related to size.

4.2.6. Bulk nanomaterials, nanostructured materials, and mixtures

Macroscopic composite materials, which contain objects at the nanoscale, may have been deliberately engineered to create novel properties. Examples of this kind of material are carbon nanotubes introduced in a polymer matrix to make it conductive, nanocomposite steel alloys which are engineered to withstand extremely high loads, and other everyday products such as rubber containing carbon black (for car tyres).

Likewise, integrated electronic circuits and, for example MEMS (Micro-Electro-Mechanical Systems) and electronic displays may today include features in the nanoscale regime, however in a much more structured way.

Such composite and electronics products, as well as other materials such as nanoporous materials, are in some definitions considered as nanomaterials, as they incorporate nanostructures in order to modify their properties. Nevertheless, as suggested above, such bulk nanomaterials should generally not be considered in a regulatory context as it is very unlikely that the nanostructured components would ever be released as 'free' particulate nanomaterials as a result of normal use. Disposal methods of such materials might however be considered in regulation, with reference to possible release of nanoparticles.

On the other hand, a wide range of other products are based on mixtures which include deliberately added nanomaterials, in order to introduce or enhance effects due to the particular properties of nanomaterials. Well known examples here are cosmetics and sunscreens, but also paints, cleaning products and lubricants can contain nanomaterials. Such products are usually not perceived as nanomaterials but as mixtures containing nanomaterials. This point of view is also adopted in the Cosmetic Products Regulation (see Chapter 2) which includes a 'nano' labelling obligation for ingredients present in the form of nanomaterials, i.e. the nanomaterial is here considered as an ingredient and not the end-product.

The considerations made so far do not distinguish the origin of a nanomaterial, i.e., whether a nanomaterial is produced (intentionally or non-intentionally) or whether it is of natural origin like many atmospheric aerosol particles. In case of

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[46] Ehara, K., Sakurai, H., 'Metrology of airborne and liquid-borne nanoparticles: current status and future needs', *Metrologia*, 47, S83-S90 (2010).

[47] Kreyling, W. G., Semmler-Behnke, M., Chaudhry, Q., 'A complementary definition of nanomaterial', *Nano Today*, available online 5 May 2010, ISSN 1748-0132, DOI: 10.1016/j.nantod.2010.03.004 (http://www.sciencedirect.com/science/article/B82X8-500Y5S6-1/2/8cf8213480d19b710d3c9683d1eb2116)

[48] ISO 9277:1995 Determination of the specific surface area of solids by gas adsorption using the BET method.

specific regulations, it may well be reasonable to make such distinctions, including attributes such as 'engineered' or 'manufactured'. Processing or other treatment of materials, as for example applied in the food industry, may also yield substructures at the nanoscale (e.g. milk and mayonnaise). Such processing may already have been used since many decades and it is questionable whether the resulting substructures, as they may occur in food matrices, should be considered as nanomaterials. For this reason specific limitations with regard to a general definition may be necessary in certain sectors. For example for the food sector, the specification 'engineered nanomaterial' would efficiently exclude traditional nanostructured components, such as those in homogenised milk and mayonnaise.

The terms '*material*' and '*nanoscale*' should both be defined in order to enable the legal enforceability of a definition. This requires the introduction of clear nanoscale limits and instructions on how such limits can be applied for nanoscale materials with size distributions. Size-related properties, nanoscale materials incorporated in a matrix and the origin of the material are also points to be considered.

4.3. Physico-chemical properties

4.3.1. Scalable versus non-scalable properties

In addition to geometric properties like size, surface area and shape, a nanomaterial can be characterised by its physico-chemical properties, as any other material. This may become crucial if an upper size limit (for example 100 nm) specified in the nanoscale definition would be too restrictive to capture all materials that exhibit specific properties due to their structure in the nanoscale. Some of these properties scale in proportion to the size, whereas others can change dramatically, as compared to those of the bulk material, when the size becomes small enough. The first category of these properties is here called 'scalable', while the second is called 'non-scalable'. Taking, for example, the particle diameter as a characteristic measure of the size of a particle, an example of a scalable property is the specific surface area (i.e. surface area per unit mass), which is proportional to the inverse of the diameter for spherical nanoparticles.

Scalable properties change continuously and smoothly with size, and therefore no size limit can be given at which a sudden change in properties could be used to identify a material as a nanomaterial, although scalable properties may also show a drastic increase below a certain size. On the other hand, there is obvious concern that scalable properties (e.g. specific surface area) become relevant for modified behaviour of nanomaterials with respect to coarser grained materials, e.g. when the size of a nanoparticle becomes comparable to a typical length scale of biological structures with which it may interact. An example is the translocation of nanoparticles through biological barriers (lung, gut, skin, blood brain barrier, placenta, etc.) or their incorporation into cells through cell membranes. These effects may be due to the size of the particles alone, or both the size and material properties, or a combination of size and specific chemical characteristics of the particle surface. If a nanoparticle acts as a carrier of substances it could mediate their translocation within an organism to places which may not be reachable easily by the substance alone. In addition to effects due to a larger specific surface area, this may lead to enhanced substance transport into cells being a direct consequence of the particle size.

Although a material may not necessarily show true nanoscale features, it can have properties that are clearly different from those of the bulk just because reducing size may lead to certain effects when the particle size becomes comparable to typical biological length scales where relevant processes of living systems occur.

4.3.2. The role of non-scalable properties and confinement effects

Non-scalable properties on the other hand are those which exhibit unique nanoscale features below a certain size. Examples include confinement effects such as the increased bandgap of semiconductor nanoparticles - quantum dots - such as lead selenide (PbSe), cadmium selenide (CdSe) and cadmium sulfide (CdS), which increases dramatically for diameters below 5 nm, or thermal properties such as the melting point of indium and tin nanoparticles, which decreases exponentially below a diameter of 15 nm[5].

Non-scalable properties include also solubility and phase transformations which depend on the surface tension, the scaling of which changes pronouncedly from the classical behaviour for particle sizes below 25 nm. A few proposed definitions, for example the Cosmetic Products Regulation[15], incorporate insolubility and/or (bio)persistence in the definition of nanomaterial, although increased solubility is a true nanoscale feature for some materials. Size-dependent crystallinity also affects the interface properties of nanoparticles, such as adsorption capacity, surface reaction rates, catalytic properties and redox potential, which can mediate molecular processes relevant for cell functions. For example, titania (TiO_2) has a structure- and size-dependent photocatalytic activity, which goes through different maxima between 25 nm and 7 nm for different reactions. Gold nanoparticles smaller than 3 nm show a high catalytic activity for certain reactions, even though bulk gold is inert. Genuine nanoscale biological effects of nanoparticles, such as generation of reactive oxygen species, are typically found at sizes of 30 nm and below.

These examples illustrate that the size at which genuinely nanoscale properties are observed depends strongly on the material, and although most of these effects appear at sizes of 30 nm and below, no general limit can be given. Furthermore, case-by-case studies are necessary for every material, since there is no direct, material-independent relationship between size and novel effects or functions.

Another problem concerning the use of physicochemical properties other than size for definition purposes is the fact that even though nanoscale properties can be found at a certain size, the distinction between nanoscale and macroscopic properties may not be as clear as it appears at first sight, because the correspondence principle in quantum mechanics states that the behaviour of systems reproduces classical physics in the limit of large quantum numbers. This means that even for typical characteristic nanoscale properties it could be difficult to decide when the property in question is really different from the bulk, i.e. where to establish the limit between nanoscale and macroscopic properties.

There is no direct, material-independent relationship between size and novel effects or functions. Therefore, no general size limit can be given below which true nanoscale properties are observed.

4.3.3. Matrix effects

The physical and chemical properties of the surrounding environment of a nanomaterial can have a substantial impact on the material behaviour. Such effects are known as matrix effects. They become especially important when looking at potential effects of nanomaterials on biological systems.

Due to their high specific surface area, particulate nanomaterials have a much higher free surface energy as compared to bulk material, which usually makes them thermodynamically unstable or metastable. In order to reduce their free energy, they often have the tendency to agglomerate or aggregate, thus decreasing their specific surface area, or to react with other substances. Nanomaterials in contact with a matrix, such as a liquid, will cause ions and polar constituents to arrange themselves in the vicinity of their surface. Depending on the chemical characteristics of the surface, the surrounding matrix, and the pH of the liquid, a nanomaterial will be charged in an ionic solution and surrounded by a shell of oppositely charged ions. This surface charge will, in turn, stabilize the nanomaterial against agglomeration. Furthermore, it will attract molecules from the liquid which are able to reduce the particle free energy. Such effects are used to keep nanoparticles well dispersed in a suspension.

Another consequence of the interaction between a nanomaterial and a liquid environment is the possibility of dissolution of certain materials, for example metal oxides. According to the Gibbs-Thomson relation, the saturation solubility is a function of the particle size and increases with decreasing particle diameter. Therefore, smaller nanoparticles will have a stronger tendency to dissolve. On the other hand, nanoparticles can also act as nuclei for heterogeneous crystallization and thus re-crystallise with the result of yielding bigger particles, a phenomenon well known from aerosol physics.

In a biological environment nanomaterials can interact with biomolecules via physical or chemical interactions in order to reduce their free energy. It is well known that in biological fluids a 'corona' of biomolecules is formed around a nanoparticle as a consequence of this interaction. This effect is believed to be very important for potential toxic effects. It has been suggested that the nanomaterial as such does not constitute the effective unit for nanomaterial-cell interaction, but rather it is the particle combined with its specific 'corona' of proteins from serum or other body fluids that reacts with the cell. Furthermore, the effective surface charge of a nanomaterial (which is the direct consequence of the interaction between the nanomaterial and the surrounding matrix) could be an important parameter relevant for its behaviour in living organisms, concerning for example the penetration of biological barriers and subsequent uptake in organs.

The behaviour of nanomaterials may be strongly influenced by the close contact with constituents of a surrounding matrix, and their apparent properties may be matrix dependent.

4.3.4. Problems related to nanoscale properties included in a definition

If a definition of 'nanomaterial' is to be based on specific nanoscale properties, it would be essential to clearly list and describe those properties and to distinguish them from bulk properties. Furthermore, a definition based on a comparison to the equivalent bulk material is not feasible as it assumes that all material exists also in the bulk form. This is not the case, particularly not for more advanced nanomaterials like the nanocarriers discussed above. Since the majority of true nanoscale properties appear at sizes of 30 nm and below, such an upper size limit would appear to be sufficient and the upper limit of 100 nm that is used in many existing definitions appears to be arbitrary. On the other hand, a size limit of 30 nm would exclude (as in the case of the 100 nm limit) a large number of materials from the definition; in particular agglomerates and aggregates of smaller nanoparticles as well as more complex forms such as nanocarriers or other materials specifically designed at the nanoscale, especially taking into consideration the so-called next generation nanomaterials.

Therefore a definition which is based on nanoscale properties in addition to size would have to precisely describe their nature, their occurrence and the measurement processes to determine them. This would lead to an increased complexity of the definition, where the measurement process of the property becomes an essential element and a critical issue with regard to the enforceability for regulatory purposes. Since there is no direct and universal property to describe novel effects or functions which appear in the nanoscale, size, or quantities derived from size, can be regarded as the only common 'property' of objects in the nanometre region.

Nanomaterials can have physico-chemical properties different to those of bulk materials. Some of these properties can be extrapolated from the macroscale, whereas others change their characteristics drastically at a certain size (true nanoscale features). Although a material may not necessarily show true nanoscale features, it can have properties that are clearly different from those of the bulk just because of its reduced size. Therefore, a definition for nanomaterials must encompass both properties deriving from pure downscaling and true nanoscale features. Since there is no unique relationship between size and physico-chemical properties which is valid for all materials, the only feature common to all nanomaterials is the nanoscale.

5. Conclusions

In view of the need of a definition of 'nanomaterial' for regulatory purposes, the considerations in this report give much attention to the applicability of a definition in a broad spectrum of regulations and directives. This must also be seen in the context of the increased public concern related to nanotechnology and the ongoing debate on potential health effects and unknown environmental impact. For this reason a single, science based definition, which is unambiguous and enforceable on the one hand, and comprehensive with respect to the great variety of existing (and future) nanomaterials on the other hand, would be desirable.

The report provides practical considerations which should be taken into account for the formulation of a definition of 'nanomaterial' for regulatory purposes. The development and formulation of a definition requires a significant amount of expert opinion in order to cover all relevant aspects in the interest of stakeholders, such as scientists, industries, regulators and the general public. It must be emphasized that each definition will have implications within the context in which it is used. A definition will thus involve policy choices (and accordingly entail political decisions) regarding the range of materials to be regulated, the broadness of scope and applicability of the definition, and its enforceability in legislation. A definition aimed for regulatory purposes should target a class of material which requires specific attention. Hence, the more specific term 'particulate nanomaterial' is considered to be more appropriate since macroscopic materials with internal structures at the nanoscale, also often denoted as nanomaterials, are not of concern in this context.

A single definition with broad applicability should be clear and easily understandable across different fields of application, and in different industrial sectors, but also must be scientifically sound. Due to the need of wide applicability, it should be rigorous and should not be limited to the scope of a specific regulation. In view of a future legal implementation of the definition and its enforceability, it is essential that terms such as 'of the order of', 'approximately', 'may show novel properties', etc., and similar imprecise expressions are avoided.

The following schemes for a single definition of 'particulate nanomaterial' are envisaged:

1. Size-based (scale)

2. Nanoscale properties-based

3. Combination of size and nanoscale properties based.

Although it may be appealing to refer in a definition to specific nanoscale properties (schemes 2 and 3) that are not observable in the bulk material (if a bulk analogue exists at all), this is not a straightforward approach. On the contrary, for pragmatic reasons and for the sake of uniqueness, broadness, clarity and enforceability, it is advantageous not to include properties other than size in a basic definition. However, specific physico-chemical properties may be relevant in the scope of a particular regulation, and therefore it should be possible to adapt the general definition to the needs of a specific implementation.

Problems occur with respect to the determination of any property used, size included. In all cases, accurate and reliable measurement methods are indispensible, and sound measurement protocols and standardisation of methods are necessary to avoid ambiguity, in particular, if a property is to be measured by relying on diverse physical principles.

The identification of a nanoscale range is likely to cause considerable controversy. Whereas the lower limit of 1 nm is probably broadly acceptable, the upper limit determines which materials will be subjected to special consideration in regulation. It will be the task of the regulatory body to establish this upper limit which will probably require a stakeholder consultation process involving academia, regulatory bodies, industries and possibly NGOs.

For a definition aimed for regulatory purposes the term 'nanomaterial' in its current general understanding is not considered appropriate. Instead, the more specific term 'particulate nanomaterial' is suggested.

The term 'material' is proposed to refer to a single or closely bound ensemble of substances at least one of which is a condensed phase, where the constituents of substances are atoms and molecules.

For a basic and clear definition of 'particulate nanomaterial', which is broadly applicable and enforceable, it is recommended not to include properties other than size.

For the size range of the nanoscale, a lower limit of 1 nm and an upper limit of 100 nm or higher should be chosen.

The questions of size distribution, shape, and state of agglomeration or aggregation, may need to be addressed specifically in subsequently developed legislation. It is also likely that certain particulate materials of concern that fall outside a general definition might have to be listed in specific legislation.

Additional qualifiers, like specific physico-chemical properties or attributes such as 'engineered' or 'manufactured' may be relevant in the scope of specific regulations.

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Appendix

Table A1 Overview of nanoscales used in existing working definitions.
All scales refer to at least one dimension except for the UK (DEFRA) which refers to 'at least two dimensions'.

Organisation/Country	Nanoscale	Ref. in text
ISO-CEN	Approximately 1 nm to 100 nm	3.1
OECD	Typically between 1 nm and 100 nm	3.2.1
EU SCENIHR	In the order of 100 nm or less	3.2.2
EU SCCP	In the order of 100 nm or less	3.2.3
EU (Cosmetic Products)	1 nm to 100 nm	3.2.4
EU (Novel Foods)	In the order of 100 nm or less	3.2.5
ACC	Typically between 1 nm and 100 nm	3.2.6
Australia (NICNAS)	Typically between 1 nm and 100 nm	3.3.1
Canada	1 nm to 100 nm	3.3.2
Denmark	In the 1-100 nm range	3.3.3
The UK	Less than 100 nm	3.3.4
The UK (DEFRA)	Up to 200 nm (in two or more dimensions)	3.3.4
US-EPA	Generally, but not exclusively, below 100 nm and above 1 nm	3.3.5

Table A2 Data of Table A1 sorted according to nanoscale.

Nanoscale	Organisation/Country
1 nm - 100 nm	EC (Cosmetics), Canada
~ 1 nm - ~100 nm	ISO-CEN, OECD, ACC, Australia (NICNAS), Denmark, US-EPA
≤ 100 nm	UK
< ~100 nm	EU SCENIHR, EU SCCP, EU (Novel Foods)
≤ 200 nm	UK (DEFRA)

Table A3. Overview of existing working definitions of 'nanomaterial'.
Given size scales have been replaced by the word 'nanoscale' for ease of comparison.

Organisation/Country	Nanomaterial	Ref. in text
ISO-CEN (draft)	Material with any external dimension in the nanoscale or having internal or surface structure in the nanoscale	3.1
OECD	Material which is either a nano-object or is nanostructured	3.2.1
EU SCENIHR	Any form of a material composed of discrete functional parts, many of which have one or more dimensions in the nanoscale.	3.2.2
EU SCCP	Material with one or more external dimensions, or an internal structure, in the nanoscale, which could exhibit novel characteristics compared to the same material without nanoscale features.	3.2.3
EU (Cosmetic Products)	An insoluble or biopersistant and intentionally manufactured material with one or more external dimensions, or an internal structure, in the nanoscale.	3.2.4
EU (Novel Foods)	Any intentionally produced material in the nanoscale or is composed of discrete functional parts, either internally or at the surface, many of which have one or more dimensions in the nanoscale.	3.2.5
ACC	An Engineered Nanomaterial is any intentionally produced material in the nanoscale.	3.2.6
Australia (NICNAS)	Industrial materials intentionally produced, manufactured or engineered to have specific properties or specific composition, in the nanoscale.	3.3.1
Canada	Manufactured material at or within the nanoscale in at least one spatial dimension, or is smaller or larger than the nanoscale in all spatial dimensions and exhibits one or more nanoscale phenomena.	3.3.2
Denmark	Materials having structures in the nanoscale.	3.3.3
The UK	Materials having structured components in the nanoscale.	3.3.4
The UK (DEFRA)	Materials in the nanoscale and are deliberately engineered i.e. not natural or unintentional by-products of other processes, and are 'free' within any environmental media at any stage in a product's life-cycle.	3.3.4
US-EPA	Engineered nanoscale material is any particle, substance, or material that has been engineered to have one or more dimensions in the nanoscale.	3.3.5

Table A4. Overview of elements in existing working definitions.
'x' indicates included element and '-' not included.

Organisation/Country	Material (m) / substance (s)	Size scale	Properties, general	Properties, specific	Manufactured/ engineered/ intentional	Also internal structure
ISO-CEN (draft)	m	x	-	-	-	x
OECD	m	x	-	-	-	x
EU SCENIHR	m	x	-	-	-	x
EU SCCP	m	x	x	-	-	x
EC (Cosmetic Products)	m	x	-	x	x	x
EU (Novel Foods)	m	x	-	-	x	x
ACC	m	x	-	-	x	-
Australia (NICNAS)	m	x	x	-	x	-
Canada	m, s	x	x	-	x	x
Denmark	m	x	x	-	-	x
The UK	m	x	-	-	-	x
The UK (DEFRA)	m	x	-	-	x	-
US-EPA	m, s	x	-	-	x	-

List of abbreviations

ACC	American Chemistry Council
ANSI	American National Standards Institute
ASTM	American Society for Testing and Materials
CEN	European Committee for Standardisation
DEFRA	Department for Environment, Food and Rural Affairs
DLS	Dynamic Light Scattering
EC	European Commission
EP	European Parliament
EPA	US Environmental Protection Agency
EPO	European Patent Office
EU	European Union
IEC	International Electrotechnical Commission
IES	Institute for Environment and Sustainability
IHCP	Institute for Health and Consumer Protection
IRMM	Institute for Reference Materials and Measurements
ISO	International Organisation for Standardisation
IUPAC	International Union of Pure and Applied Chemistry
JWG	Joint Working Group
NICNAS	National Industrial Chemicals Notification and Assessment Scheme
NSP	Nanotechnology Standards Panel
OECD	Organisation for Economic Co-operation and Development
REACH	Registration, Evaluation, Authorisation and Restriction of Chemical substances
SCCP	Scientific Committee on Consumer Products
SCENIHR	Scientific Committee on Emerging and Newly Identified Health Risks
TC	Technical Committee
TS	Technical Specification
TSCA	Toxic Substances Control Act
UK	United Kingdom
WG	Working Group
WPMN	Working Party on Manufactured Nanomaterials
WPN	Working Party on Nanotechnology

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Title: **Considerations on a Definition of Nanomaterial for Regulatory Purposes**

Authors: Göran Lövestam*, Hubert Rauscher**, Gert Roebben*, Birgit Sokull Klüttgen**,
Neil Gibson**, Jean-Philippe Putaud*** and Hermann Stamm**
*IRMM, **IHCP, ***IES

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Abstract

The recent EU Cosmetic Products Regulation includes a labelling obligation for nanomaterials in the list of ingredients, in order to allow consumers to make a choice. Similar provisions are now being considered for other regulations/directives, e.g. the Novel Foods Regulation. Also the European chemicals legislation REACH may need adjustments to address and control the potential risk of nanomaterials. The introduction of these provisions specific to nanomaterials requires the adoption of a definition of the term ‘nanomaterial’. This need is also acknowledged by the European Parliament which has called for a comprehensive science-based definition in Community legislation.

The report reviews and discusses issues related to a definition of the term ‘nanomaterial’. It gives a short overview about what may be considered as nanomaterials, their novel properties and applications. The need for a definition of nanomaterial is discussed, and the question of what should be achieved by a definition is addressed. The report gives an overview of definitions by international, national and European institutions, and lists approaches used in European legislation. It summarises the advantages and shortcomings of different elements typically used in available definitions, regarding their applicability in a regulatory context.

The report concludes that a definition of the term ‘nanomaterial’ for regulatory purposes, only should concern ‘particulate nanomaterials’. The definition should ideally be broadly applicable in EU legislation and in line with other approaches worldwide. The following three key elements are identified as being crucial: (i) the term ‘material’, (ii) the nanoscale, and (iii) specific nanoscale properties. ‘Material’ and ‘nanoscale’ should both preferably be defined precisely in order to ease enforceability. This implies the introduction of precise nanoscale limits and instructions on how such limits can be applied to nanoscale materials with size distributions. For a basic and clear definition, which is broadly applicable and enforceable, it is recommended not to include properties other than size in a general definition. Shape and state of agglomeration/aggregation must be adequately dealt with either in the definition or in subsequent legislation. Other issues may need to be considered in specific regulations such as origin of the nanomaterial, properties other than size, and specific inclusion or exclusion of certain nanomaterials.

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