Nanomaterials within an Advanced Materials Framework: Definitions, Regulation, and Sustainability

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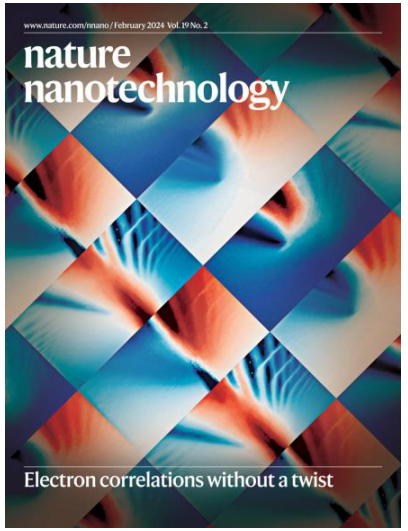
European Commission JRC

EU-U.S. CoR Workshop, Dübendorf (CH), 16 October 2024

European Commission

This Presentation

- Are nanomaterials advanced materials?
- Global nanomaterial definitions – parameters
- Challenges
- Definitions, examples
- Safety and Sustainability



Comment

https://doi.org/10.1038/s41565-023-01578-x

How nanoparticles are counted in global regulatory nanomaterial definitions

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Check for updates

The legal definition of a nanomaterial differs around the world, meaning that the same material may be classified as a nanomaterial, or not, depending on the country where it is classified. The first steps towards converging on an international definition are to recognize the differences between existing nanomaterial definitions and to agree on particle counting methods. Meanwhile, we propose a naming convention that indicates the key criteria of a specific definition of a nanomaterial.

From a regulatory point of view, nanomaterials are generally considered to be materials with features between 1 and 100 nanometres. These materials have been associated with possible nanometre-scale-specific safety issues[1], triggering a global effort to set specific regulatory requirements. Legislators have established nanomaterial definitions that are country- or region-specific so that, potentially, the same material may be classified as a nanomaterial, or not, depending on the definition used. Whether a material is regarded as a nanomaterial or not in a legal context may impact, for example, the data requirements.

Here we examine the (main) differences between the definitions in the various jurisdictions, how to achieve a global definition, and propose a way forward. In this Comment, we provide an overview of whether and how nanomaterials are defined or described in the chemicals legislation or guidance in the Organisation for Economic Co-operation and Development (OECD) member countries, the European Union (EU) and other relevant economies. We highlight how differences between the definitions affect which materials are considered to be nanomaterials. We discuss whether international convergence could be achieved. Finally, we propose a generalized naming convention that can be applied to any specific definition of nanomaterial.

A multitude of regulatory nanomaterial definitions

A definition of a nanomaterial for international technical application is provided by the International Organization for Standardization (ISO) (Table 1). It does not explicitly refer to particles, nor does it include a quantitative threshold of the fraction of material that must be at the nanoscale for the whole material to be considered a nanomaterial. Therefore, the ISO definition is not suitable for regulatory purposes, because most real-life particulate materials are mixtures of nanometre-sized and non-nanometre-sized particles and contain particle agglomerates and/or aggregates.

The OECD agreed on a size-based working definition of a nanomaterial to be used for the sole purpose of its Working Party on Manufactured Nanomaterials (WPMN) in order to progress discussions of regulatory needs and to develop methodological support for nanotechnologies. The OECD published a Council Recommendation[2] that concludes that the management of the possible risks of nanomaterials is covered by existing regulatory frameworks for chemicals.

These developments helped legislators globally to define the term 'nanomaterial' clearly for each country's chemicals legislation. However, it is challenging to achieve global convergence of these definitions of nanomaterial[3,4]. Additionally, there are different approaches to what makes a definition 'legal', how something should be 'regulated' and whether regulatory needs are sufficiently addressed by guidance, guidelines or standards instead of legislation. Moreover, different jurisdictions apply different underlying conceptual principles for the safety assessment and management of chemicals. This leads to considerable differences regarding the meaning of the term nanomaterial in legal contexts.

Identifying and counting nanoparticles

Most nanomaterial definitions require that particles at the nanometre scale are identified and counted. Regulatory definitions may include a quantifiable threshold of the fraction of particles that must be at the nanometre scale, in which case quantification of particles is essential[5–7]. The particle size measured depends on the method applied, the external dimension chosen to represent its size[8], and the way particles are counted[9]. The OECD Test Guideline 125 (ref. 10) includes electron-microscopy-based methods, which are the only methods that provide the information required by EU legislation to identify nanomaterials. Electron microscopy allows particles to be identified and counted. Particles can be on their own or may be constituents in aggregates (consisting of strongly bound constituent particles) and agglomerates (consisting of weakly bound constituent particles and/or aggregates). It furthermore allows the external dimensions ('size') of irregularly shaped particles[8] to be measured and the size distribution to be evaluated.

However, even starting from the same electron micrograph, the resulting number of particles and size distribution can change spectacularly depending on how the particles are counted[9]. Figure 1 illustrates different ways of counting agglomerated and aggregated particles according to different definitions of a nanomaterial. This is a key reason for differences in classification as a nanomaterial in different legal contexts.

Table 1 reviews the legislative texts by region and the major aspects of each nanomaterial definition. The following countries use the ISO definition and are not listed in Table 1: South Africa, Thailand and China. Other countries, such as Argentina, Brazil, Chile and Colombia, do not currently define nanomaterials in either their chemicals legislation or guidance.

nature nanotechnology

Rasmussen, Riego, Rauscher, *Nature Nanotechnology* **volume 19**, pages132–138 (2024)

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Are Nanomaterials Advanced Materials?

From the OECD working description of advanced materials

OECD
Organisation for Economic Co-operation and Development

ENV/CBC/MONO(2022)29

[…] AdMa are understood as materials that are rationally designed to have

- new or enhanced properties, and/or
- targeted or enhanced structural features

with the objective to achieve specific or improved functional performance. This includes both new emerging manufactured materials, and materials that are manufactured from traditional materials. This also includes materials from innovative manufacturing processes that enable the creation of targeted structures from starting materials, such as bottom-up approaches. It is acknowledged that what are currently considered AdMa will change with time […]

B. Giese, et al, Advanced Materials: Overview of the Field and Screening Criteria for Relevance Assessment, Umweltbundesamt, 2020

F. A. Monikh, et al., "Advanced materials" and the challenges on the horizon for testing their (eco)toxicity and assessing their hazard, Environ. Sci.: Adv., 2023, 2, 162

incl nanomaterials

See also: Advanced Materials journal & AMI2030 manifesto -> ✓

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Global nanomaterial definitions - parameters

Globally, nanomaterials are described by

Size range: 1 nm to 100 nm (mostly)

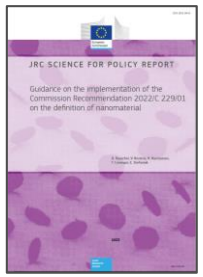
Particle type: Manufactured, Incidental, Naturally occurring, N/A

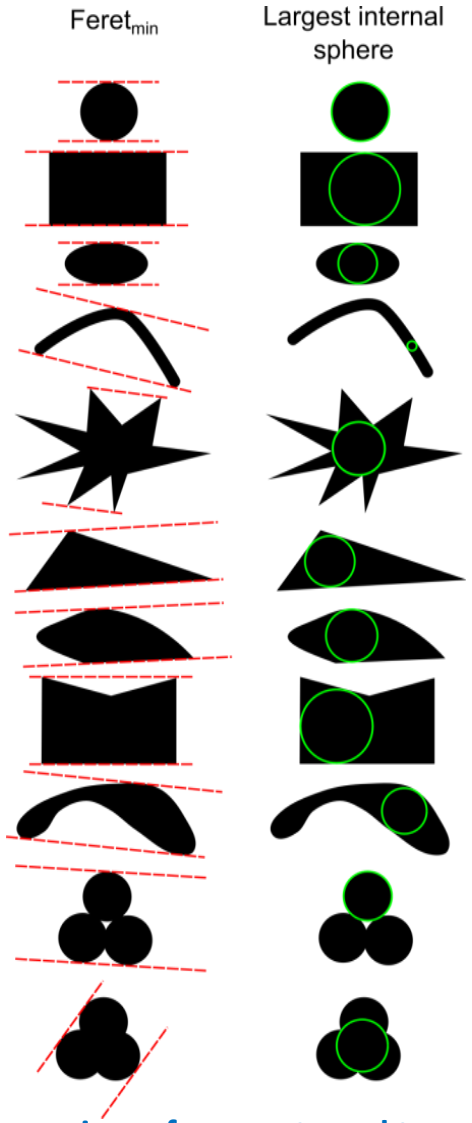
Metric used: Particle number, Weight, N/A

Threshold: Number-based %, Weight-based %, Not specified

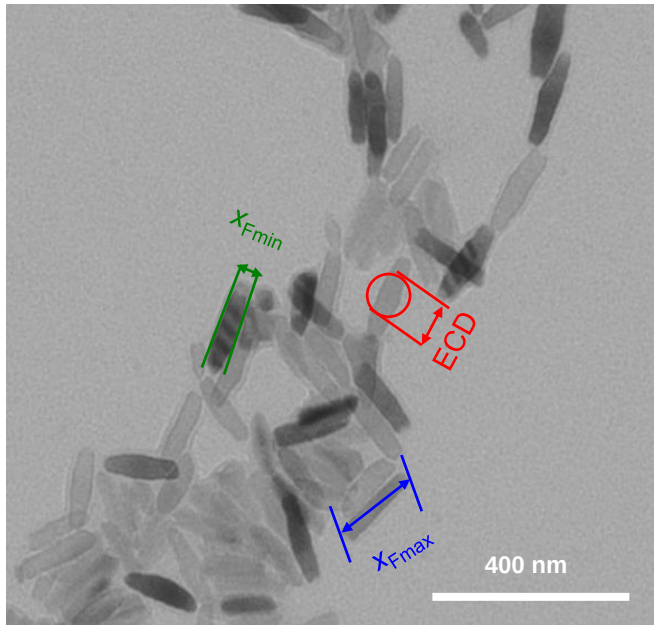
Additional aspect: Must have at least one unique and novel property

Challenges: size and how to measure it?





- External dimensions can be represented in various ways, e.g. by the Feret diameter.
- The external dimensions of particles with irregular shape can be assessed by the minimum Feret diameter and/or the maximum inscribed circle diameter.



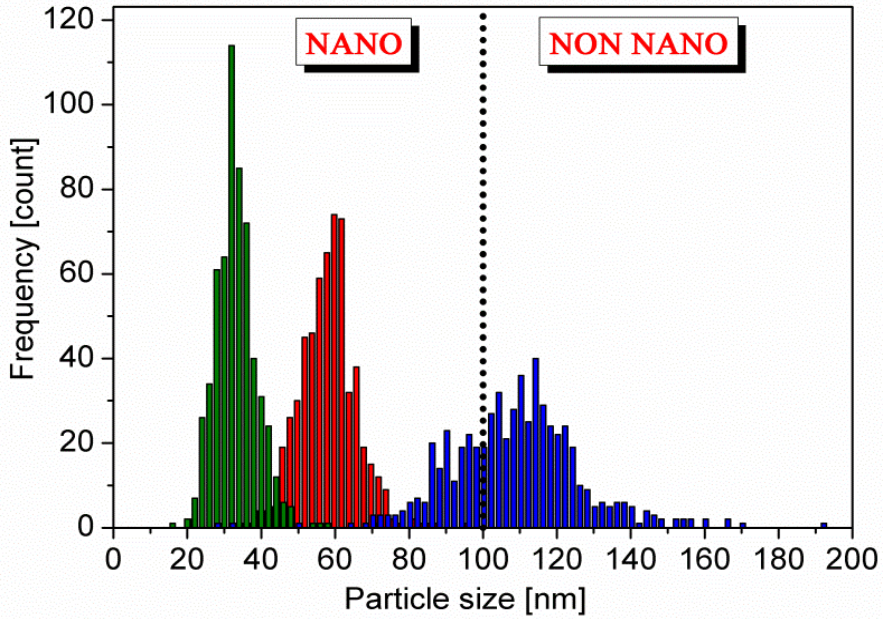


Figure: TEM micrograph of titanium dioxide nanorods with simplified representation of different particle size measurands, and corresponding number size distributions for x_{Fmin} (green), x_{Fmax} (blue) and ECD (red) (TEM image, Joint Research Centre, © European Commission).

Rauscher et al., An overview of concepts and terms used in the European Commission's definition of nanomaterial, doi:10.2760/459136
Rauscher et al., Identification of nanomaterials through measurements, doi:10.2760/7644, JRC118158.
Rauscher et al., Guidance on the implementation of the Commission Recommendation 2022/C 229/01 on the definition of nanomaterial, doi: 10.2760/143118

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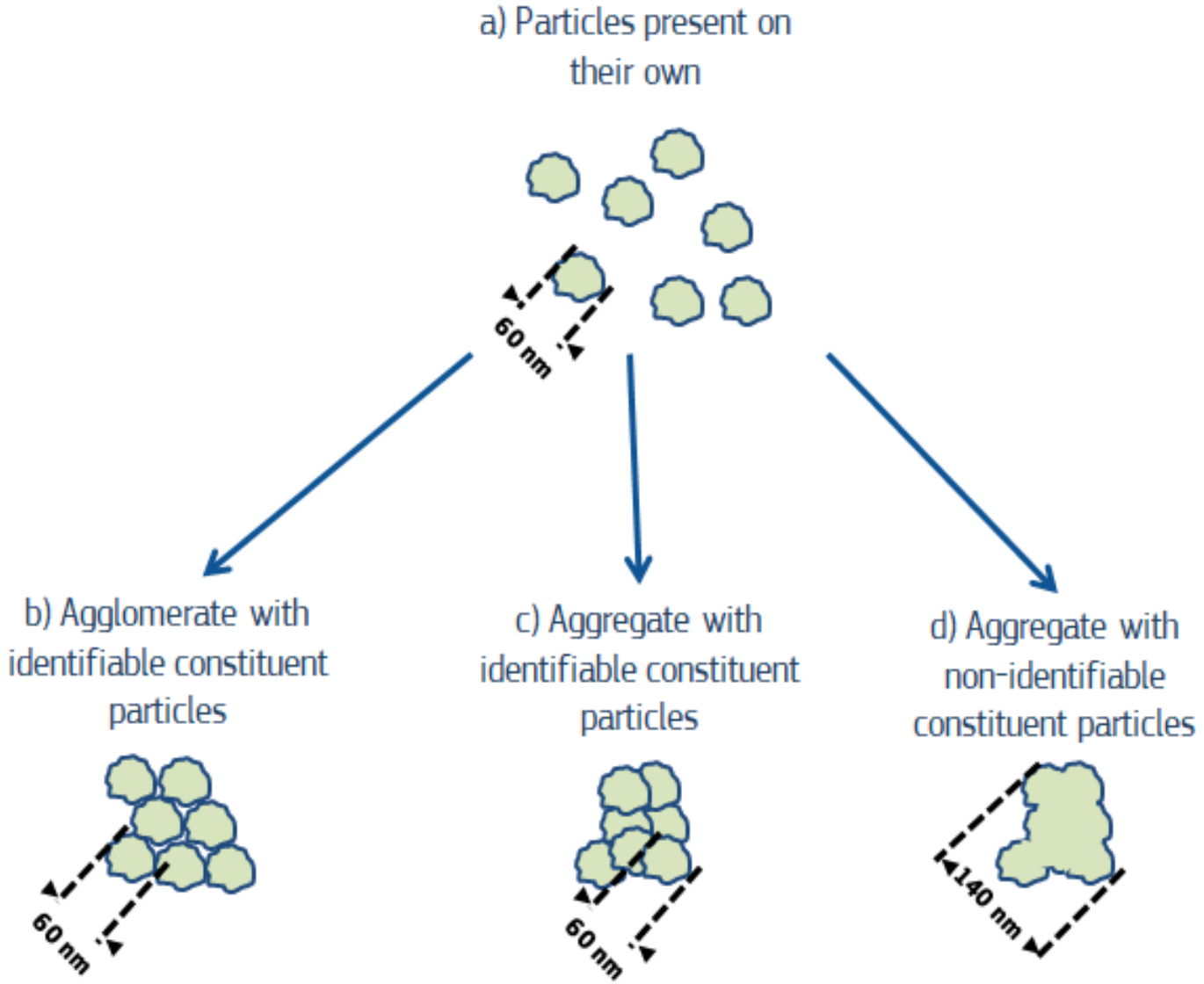
Individual particles, agglomerates, aggregates



JRC 132102

"…consisting of solid particles that are present, either on their own or as identifiable constituent particles in aggregates or agglomerates…" (EC Recommendation 2022)

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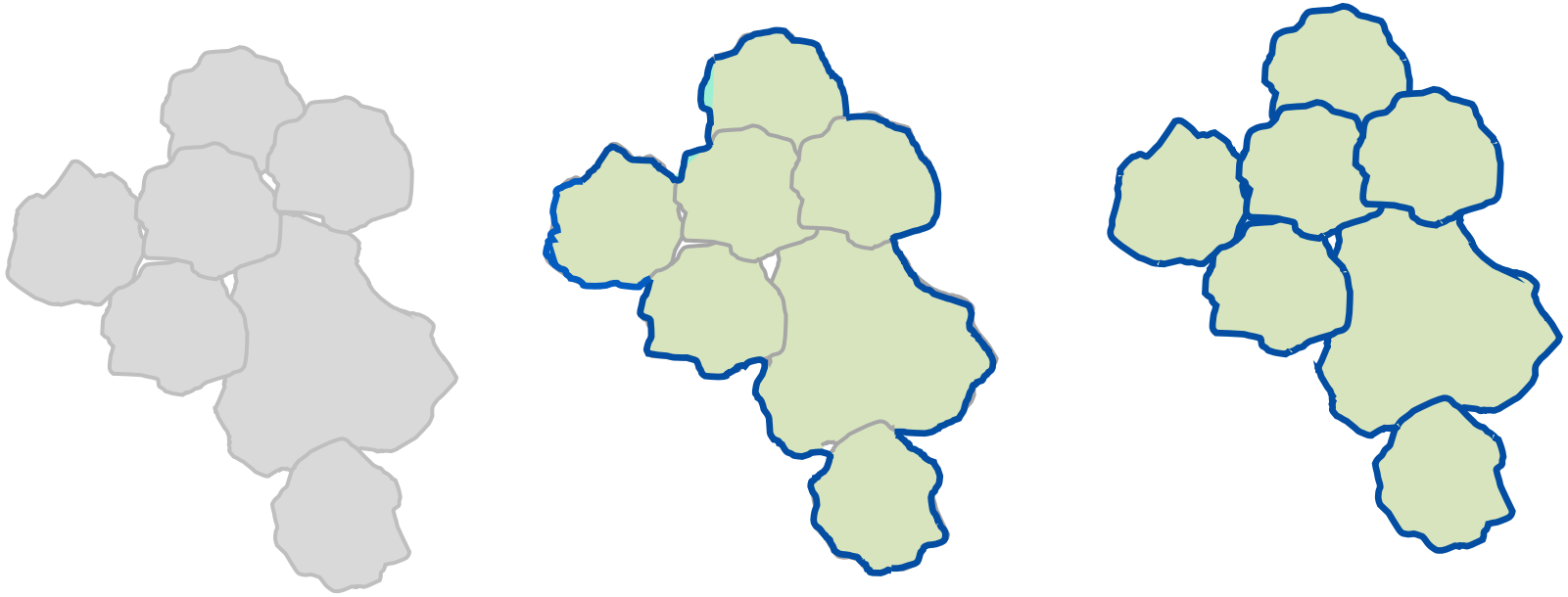
Challenges: counting agglomerates and aggregates



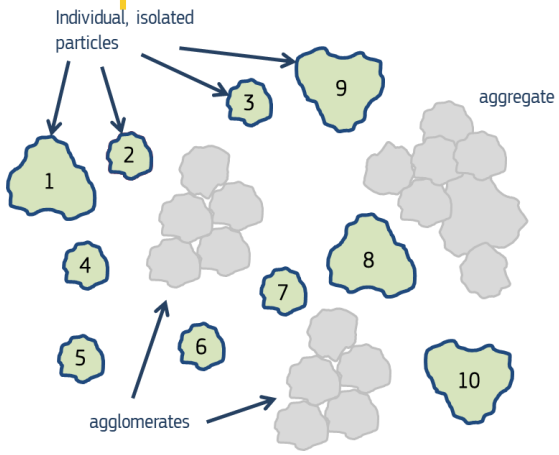
Zero particles

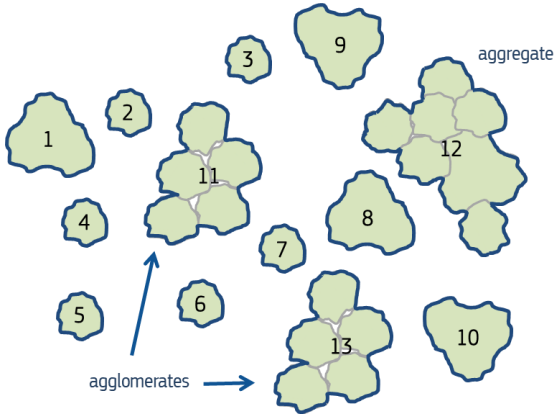
One particle

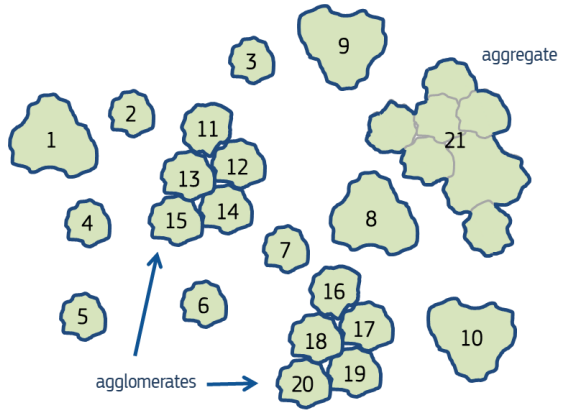
Seven particles

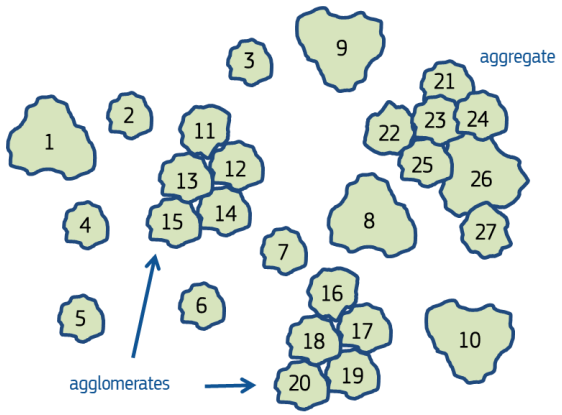
Rasmussen, Riego, Rauscher, *Nature Nanotechnology* **volume 19**, pages132–138 (2024

Challenges: Which particles to count

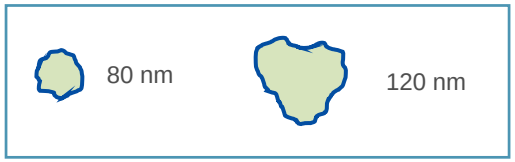








Counting rule 1
only individual / non-touching particles are counted:
10 particles



Counting rule 2
individual particles, aggregates and agglomerates are counted as one particle:
13 particles

Counting rule 3
Individual particles, aggregates, and constituent particles in agglomerates are counted as one particle:
21 particles

Counting rule 4
Individual particles and constituent particles in agglomerates and in aggregates are counted as one particle
27 particles

Bresch, Hodoroaba, Schmidt, Rasmussen, Rauscher,
Nanomaterials 12 (2022) 2238, https://doi.org/10.3390/nano12132238

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Global definitions - parameters

Globally, nanomaterials are described by

- **Size range:** 1 nm to 100 nm (mostly)
- **Particle type**: Manufactured, Incidental, Naturally occurring, N/A
- **Metric used:** Particle number, Weight, N/A
- **Threshold:** Number-based %, Weight-based %, Not specified

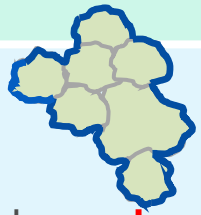
Definitions, examples

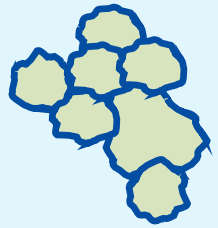
US-EPA nanomaterial rule (TSCA)*	EC nanomaterial definition (2022)**
• Chemical substances, […] that are solids at 25 °C and standard atmospheric pressure; that are manufactured or processed in a form where any particles, including aggregates and agglomerates, are in the size range of 1–100 nanometers (nm) in at least one dimension; and that are manufactured or processed to exhibit one or more unique and novel properties. • This rule does not apply to chemical substances manufactured or processed in forms that contain less than 1% by weight of any particles, including aggregates and agglomerates, in the size range of 1–100 nm. These parameters are for purposes of identifying chemical substances that are subject to the rule and do not establish a definition of nanoscale material. • Unique and novel properties are defined […]	• 'Nanomaterial' means a natural, incidental or manufactured material consisting of solid particles that are present, either on their own or as identifiable constituent particles in aggregates or agglomerates, and where 50 % or more of these particles in the number size distribution fulfil at least one of the following conditions: • (a) one or more external dimensions of the particle are in the size range 1 nm to 100 nm; • (b) the particle has an elongated shape, such as a rod, fibre or tube, where two external dimensions are smaller than 1 nm and the other dimension is larger than 100 nm; • (c) the particle has a plate-like shape, where one external dimension is smaller than 1 nm and the other dimensions are larger than 100 nm.

*TSCA reporting and recordkeeping requirements (82 FR 22088)
**EC recommendation (2022/C 229/01)

Examples of nanomaterial “definitions” from the USA and EU

Geographical area	Agglomerates and aggregates	Comments
USA **Toxic Substances Control Act (TSCA)**	Both agglomerates and aggregates are counted as one particle	Metrics: **weight** Threshold: **1%** (1-100 nm) Particle type: manufactured; must have at least one unique and **novel property**
USA **Food and Drug Administration**	Not specified	Metrics: not applicable Threshold: not specified Particle type: manufactured; is engineered to exhibit properties or phenomena, including physical or chemical properties or biological effects, that are attributable to its dimension(s), even if these dimensions fall outside the nanoscale range, up to one micrometer (1 000 nm)
EU Recommendation	The constituent particles of agglomerates and aggregates are each counted as one particle	Metrics: **particle number** Threshold: **50%** (1-100 nm) Particle type: manufactured / incidental / naturally occurring





see also *Nature Nanotechnology* **volume 19**, pages132–138 (2024)

Implementing regulatory nanomaterial definition(s):

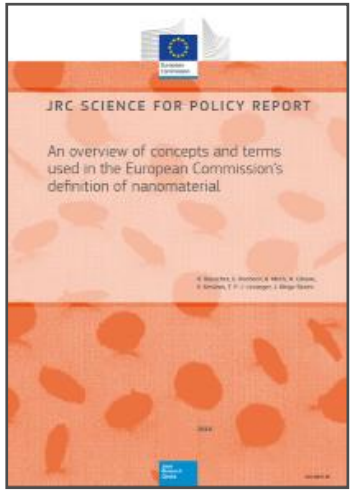
OECD Guidelines: PSD (1 nm – 1000 nm), VSSA (nano)

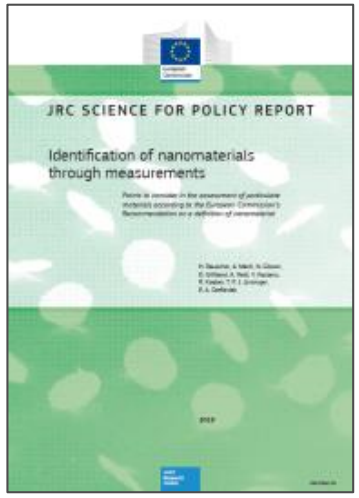
1) **OECD Test Guideline 125**: Nanomaterial Particle Size and Size Distribution of Nanomaterials
2) **OECD Test Guideline 124**: Determination of the Volume Specific Surface Area of Manufactured Nanomaterials *[relevant for EU definition]*

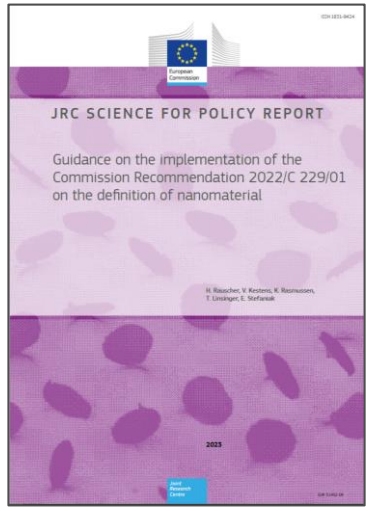
["*However, a material with a specific surface area by volume of < 6 m^2/cm^3 shall not be considered a nanomaterial*."]

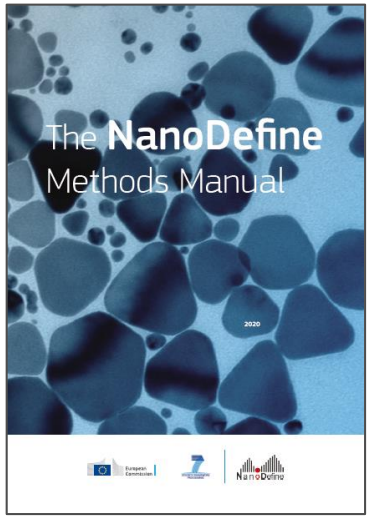
JRC Guidance

- Terms
- Methods
- Methods Manual









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Rauscher et al., Guidance on the implementation of the Commission Recommendation 2022/C 229/01 on the definition of nanomaterial, doi: 10.2760/143118
Mech et al., The NanoDefine Methods Manual, doi: 10.2760/79490

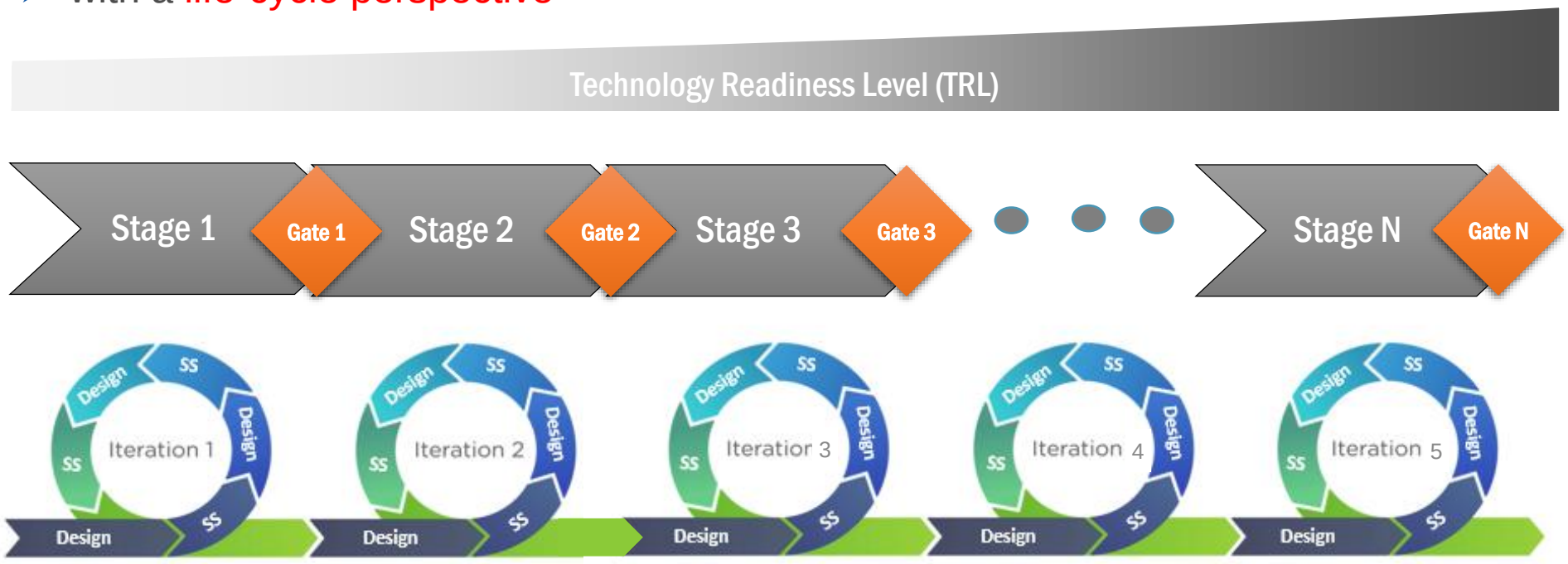
Advanced (Nano)Materials should be “Safe and Sustainable by Design”

Conclusions of the Council of the European Union, 11 October 2024

SSbD Framework*

Innovators should

- address safety, sustainability and functionality together
- from the earliest stages of innovation onwards
- with a life-cycle perspective



and **EC Recommendation (EU) 2022/2510**

*EC/JRC SSbD FRAMEWORK https://publications.jrc.ec.europa.eu/repository/handle/JRC128591

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Thank you

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Definitions, examples

Geographical area	Text of definition	How aggregates agglomerates accounted for	Comments
ISO vocabulary (1)	**Nanomaterial** **material with any external dimension in the nanoscale* or having internal structure or surface structure in the nanoscale** (Note 1: see ** for definitions of certain types of nanomaterial.) *nanoscale. length range approximately from 1 nm to 100 nm ** • engineered nanomaterial. nanomaterial designed for specific purpose or function • manufactured nanomaterial. nanomaterial intentionally produced to have selected properties or composition • incidental nanomaterial. generated as an unintentional by-product of a process. (Note 1: The process includes manufacturing, biotechnological or other processes, including natural processes. Note 2: Incidental nanomaterial is also used as a synonym for “ultrafine particle” in ISO/TR 27628:2007)	Not specified	Metrics used: N/A Threshold: Not specified Particle types: m/i/n

Rasmussen, Riego, Rauscher, *Nature Nanotechnology* **volume 19**, pages132–138 (2024

[1] ISO 80004-1:2023 Nanotechnologies –Vocabulary — Part 1: Core vocabulary.

EU legislation explicitly referring to nanomaterials (selection)

Regulatory framework	Definition	Approval procedure	Safety assessment	Labelling	Guidance
REACH (Chemicals) Regulation 1907/2006 and 2018/1881 (amended Annexes)	✓ "nanoforms"		✓		✓
Biocidal Products Regulation 528/2012	✓	✓	✓	✓	
Cosmetic Products Regulation 1223/2009	✓	✓	✓	✓	✓
Novel Foods Regulation 2015/2283	✓	✓	✓	✓*	✓
Food Additives Regulation 1333/2008			✓	✓*	✓
Plastic Food Contact Materials Reg. 10/2011		✓	✓		
Active & Intelligent FCM Regulation 450/2009		✓	✓		
Food Information Provisions Regulation 1169/2011	✓			✓	
Medical Devices Regulation EU/2017/745	✓	Conformity assessment	✓		

✓ → based on EC recommendation 2011

Currently the **cosmetic products regulation** is being updated.

* Labelling of novel foods and food additives containing nanomaterials is required under FIC Regulation 1169/2011

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The nanomaterial definition recommended by the European Commission (2022/C 229/01)

1. '**Nanomaterial**' means a natural, incidental or manufactured material consisting of solid particles that are present, either on their own or as identifiable constituent particles in aggregates or agglomerates, and where 50 % or more of these particles in the number size distribution fulfil at least one of the following conditions:

(a) one or more external dimensions of the particle are in the size range 1 nm to 100 nm;

(b) the particle has an elongated shape, such as a rod, fibre or tube, where two external dimensions are smaller than 1 nm and the other dimension is larger than 100 nm;

(c) the particle has a plate-like shape, where one external dimension is smaller than 1 nm and the other dimensions are larger than 100 nm.

In the determination of the particle number size distribution, particles with at least two orthogonal external dimensions larger than 100 µm need not be considered.

However, a material with a specific surface area by volume of < 6 m^2/cm^3 shall not be considered a nanomaterial.

exclusion criterion based on VSSA

possible cut-off for counting

Text in green highlight by the JRC

Course in the EU ACADEMY

A course ***Nanomaterials in EU Legislation*** is offered via the EU Academy (https://academy.europa.eu/)

- It has 4 modules:
  - Module 01 - Introduction to Nanomaterials
  - Module 02 - EU legislation and chemicals
  - Module 03 - How specific EU legislation addresses Nanomaterials
  - Module 04 – Nanomaterials and REACH