Nanomaterials and REACH – What do I have to do differently?

Part 2: Characterisation of nanoforms for REACH

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Characterisation of nanoforms for REACH

Regulation (EC) 1907/2006 (REACH) was updated in December 2018 to clarify the information companies placing a substance on the market as a nanomaterial need to provide as part of their REACH registration.

The changes include amendments to ANNEX VI Section 2 relating to the information needed to prove the identity of substances and require registrants to supply particle characterisation information for nanoforms of their substance. The changes have implications for anyone importing or manufacturing substances as a powder. This white paper introduces the complexities associated with characterisation of nanoforms and highlights some key techniques.

Definition: What is a nanomaterial/nanoform

The current definition of a nanomaterial/nanoform is:

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

Furthermore, the term *nanoform* is used to distinguish forms of a substance that fulfil the EC Recommendation on the definition of the term 'nanomaterial' but differ with regard to size distributions, shape and/or surface chemistry.

Therefore, in order to establish if a substance is a nanomaterial, the number of constituent particles that have at least one external dimension between 1 and 100 nm should be measured. Unfortunately, it is not a straight-forward matter to measure these parameters and a combination of different techniques and expert judgement are needed.

Constituent particles: Size, distribution and shape

Evaluation of constituent particle size distribution and shape is critical in order to define a substance as a nanomaterial and to identify the corresponding nanoform(s). Nanoparticles in suspension often exist as agglomerates/aggregates, thereby complicating measurement of constituent particle size. Aggregation/agglomeration is heavily influenced by sample preparation, highlighting the need to maintain a stable suspension of constituent particles. Sonication of the sample, addition of a stabilising agent, or adjusting pH can be effective in maintaining a population of constituent particles for the purposes of analysis.

Microscopy is a useful method for measuring constituent particle size, capable of measuring both the dimensions and shapes of individual particles. However, for a statistically significant distribution 100s of separate particles need to be measured. This process is time-consuming and introduces a risk of bias so additional techniques are often employed which can measure a size distribution.

Many of the established alternative methods measure size distribution by volume or mass rather than number (required for REACH) and typically measure the diameter of the swept area as a particle tumbles through the media (e.g. hydro/aerodynamic radius). Therefore, the measured dimension is the longest dimension plus closely associated solvent molecules.

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[1] https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32018R1881&from=EN
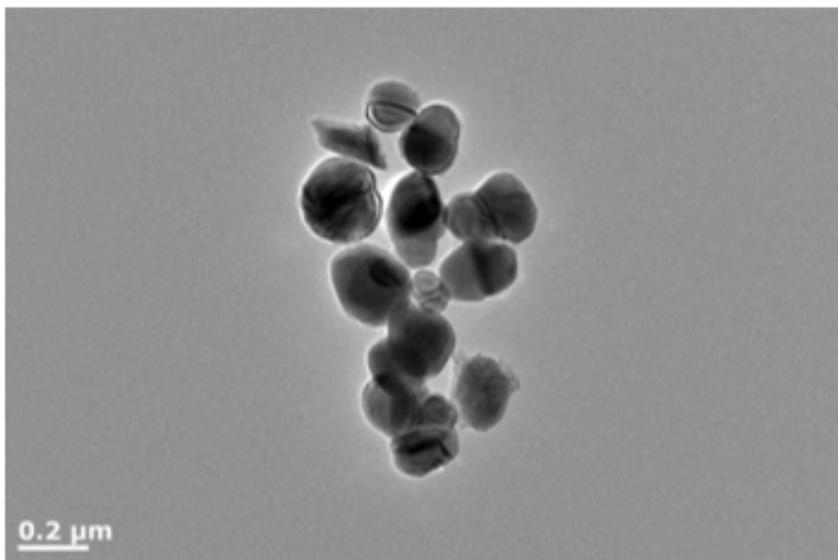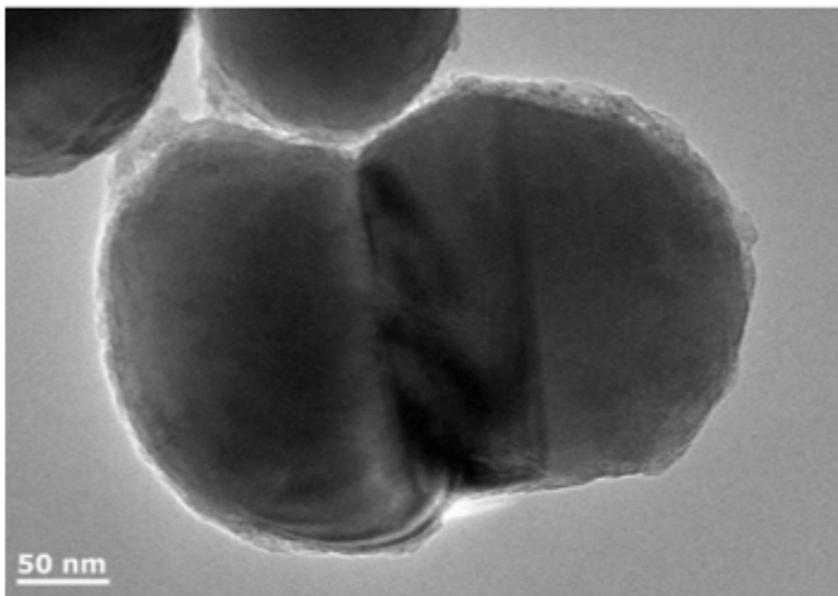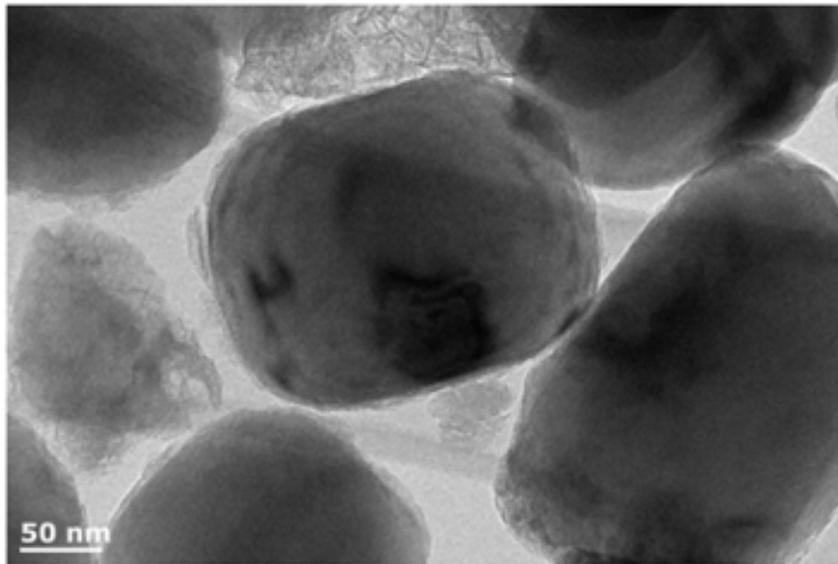
Figure 1: Transmission Electron Microscopy (TEM) images of (top) a cluster of particles, (middle) an aggregate of two constituent particles and (bottom) an agglomerate composed of both constituent particles and aggregates

Specific surface area

The Commission Recommendation of 18th October 2011 states that:

A material should be considered as falling under the definition [of a nanomaterial] where the specific surface area by volume of the material is greater than 60 m^2cm^{-3}.[2]

Brunauer-Emmett-Teller (BET) analysis is the method used to measure the Specific Surface Area. Note that the use of BET analysis in isolation is not sufficient for the purposes of defining a substance as a nanomaterial or not.

However, a material which, based on its number size distribution, is a nanomaterial should be considered as complying with the definition [of a nanomaterial] even if the material has a specific surface area lower than 60 m^2cm^{-3}.[2]

Chemical composition of nanomaterials

Most toxicological reviews of nanomaterials have shown that chemical composition is one of the primary factors influencing toxicity. The REACH regulation is performed by substance, so knowledge of the chemical composition of a nanomaterial is essential. Most of the techniques that are applicable to bulk substances are also useful for nanomaterials. The REACH regulation also requires information regarding surface functionalisation of nanomaterials, this can be derived from descriptions of the manufacturing methods used or from analytical data (or a combination).

Summary

Particle characterisation usually requires more than one analytical method and needs knowledge of the substance to choose the best available technique. Sample preparation is a key consideration that must to be taken into account in every case in order to produce representative, reproducible results. Techniques to determine chemical composition and surface functionalisation are also essential. Examples of available techniques are outlined in Appendix 1.

Once particle characterisation has been performed, the information can be used to support hazard assessment, both for REACH and for more general risk assessment. As with characterisation, the unique properties of nanomaterials can require modification of standard test protocols. These are discussed in other Yordas Group white papers.

[2] https://ec.europa.eu/research/industrial_technologies/pdf/policy/commission-recommendation-on-the-definition-of-nanomater-18102011_en.pdf

Appendix 1: Example techniques for measuring particle size and distribution, morphology, chemical composition and surface functionalisation of nanoparticles

Analytical method	What does it measure?	How it works
SEM (Scanning Electron Microscopy)	Particle size, shape, agglomeration behaviour	Uses beam of electrons that interacts with the surface of a sample to give a high-resolution image of a selected area.
TEM (Transmission Electron Microscopy)	Particle size, shape, agglomeration behaviour	Similar to SEM. Uses electrons transmitted through a thin sample.
DLS (Dynamic Light Scattering)	Hydrodynamic diameter, distribution	Calculates rate of diffusion of a particle through a solution by measuring the fluctuation in scattering intensity.
SMPS (Scanning Mobility Particle Sizing)	Particle Size	A charge is applied to an aerosol, particles sized based on their ability to traverse an electric field. Electric mobility used to estimate particle size.
CHDF (Capillary Hydrodynamic Fractionation)	Particle size, distribution, hydrodynamic diameter	Different particles move at different speeds through a capillary.
FFF (Field Flow Fractionation)	Particle size separation, hydrodynamic diameter	Chromatography based separation by rate of diffusion through a field
AUC (Analytical Ultracentrifugation)	Particle size, distribution,	Dispersed sample submitted to high centrifugal forces, radial distribution measured by NIR-Uv-vis
LALLS (Low Angle Laser Light Scattering)	Particle size and distribution	Scattering pattern of a laser fired at a wet or dry sample at a low angle compared with an optical model
SAXS (Small-angle X-ray Scattering)	Particle size and distribution	Scattering pattern of X-ray passing through a suspension
XDC (X-ray Disc Centrifuge)	Particle size, distribution, hydrodynamic diameter	Dispersed sample placed on glass rotor. X-rays fired through dispersion and attenuation proportional to concentration. Particle size measured using Stokes' Law

PTA (Particle Tracking Analysis)	Number distribution, hydrodynamic diameter	Measures Brownian motion through a medium using light scattering to track onto a single particle
XRD (X-Ray Diffraction)	Average particle size	Uses broadening of signals to measure finite diffracting domains
BET (Brunauer Emmet Teller)	Specific surface area	Measures adsorption of nitrogen onto a surface
Solid-state NMR (Nuclear Magnetic Resonance)	Surface functionalisation and composition	Uses strong static magnetic fields and radiofrequency pulses to manipulate nuclear 'spins' in a solid or semi-solid sample
FT-IR (Fourier Transform – Infrared)	Surface functionalisation and composition	Measures how a sample absorbs infrared light
Raman spectroscopy	Surface functionalisation and composition	Relies on inelastic scattering of monochromatic light in the visible, near-infrared, or near-ultraviolet range
Energy Dispersive X-ray (EDX) spectroscopy	Elemental composition	Measures the energy released upon bombarding the sample with X-rays, amount of energy released is diagnostic of the element in question
Inductively Coupled Plasma (ICP) spectroscopy	Elemental (metal) composition	Converts atoms into ions which can then be detected, for instance using mass spectrometry (ICP-MS)