

## Title: Metrology for innovative nanoparticles

### Abstract

The unique properties of nanomaterials have enabled the production of improved materials. In high performance applications of such materials, the tolerances on particle size, shape, chemistry, concentration and distribution are critical. Whilst it is possible to manufacture a wide variety of particles, the validation and quality control of these materials is beyond the means of many industries and often involves expensive analytical methods. Industry needs to have validated and useful metrological methods to measure number concentration of nanoparticles, shell thickness, and surface chemistry: highly relevant properties of nanoparticles that impinge directly upon their processing and performance in products.

### Keywords

Nanoparticle; size; size distribution; number concentration; core-shell; surface chemistry; shell thickness.

### Background to the Metrological Challenges

Highly engineered, monodisperse nanoparticles are increasingly used in commercial products due to their unique and tuneable properties. Many types of nanoparticles exist: metals used in catalysis, medical applications and conductive inks; metal oxides used in fuel cells and ferrofluids; semiconductors used as quantum dots and rods for imaging and photonics; and organic particles used as frozen ionic liquids for electronic applications, drug delivery vehicles, fluorescent reporters and advanced coatings. In these applications, one of the important measurands which defines performance is the size of the particles and, related to this, the size distribution. However, a simple size measurement is inadequate for the needs of innovative industries and additional information is required, for which the metrology is lacking.

This SRT focuses upon two of the most important and tractable problems:

- measurement of nanoparticle number concentration and;
- measurement of nanoparticle surface chemistry.

The concentration of nanoparticles in suspension is required to optimise and reproduce formulations and products. Within the framework of the EU Commission recommendation for the definition of nanomaterials (2011/696/EU), which is based upon number concentrations, it is important for industry to have a means of measuring particle number both below and above the 100 nm limit of the definition to ensure that they comply with future regulation of such materials. In many cases, this concentration is not known but is calculated upon the basis of assumptions and mass-balance considerations. There is currently a lack of validated methods that can be used to determine nanoparticle number concentrations.

The measurement of size for monodisperse, spherical particles in liquid can be readily achieved by many techniques. These include: light scattering, such as Dynamic Light Scattering (DLS); Centrifugal Liquid Sedimentation; Transmission Electron Microscopy (TEM); Atomic Force Microscopy and; emerging methods, such as single-particle ICP-MS (spICP-MS). For particles that are polydisperse the conversion of data into a number-based size distribution, or even accurate average size, is far from straightforward. This is due to the fact that few, if any, of the techniques are currently able to quantify the number concentrations of particles. Some methods have the capability to count particles individually within their liquid suspension, for example: Nanoparticle Tracking Analysis and Tuneable Resistive Pulse Sensing, but matrix effects and bias in size selectivity are untested. Others, particularly TEM and spICP-MS, have the potential to do so, once sampling biases and sample preparation issues are adequately addressed. However, the most convenient and simple method, DLS, is notoriously inaccurate. It, and other population based techniques, require both a metrological framework and calibration with appropriate certified reference materials (CRM) to achieve relative quantification of number concentrations. Electrospray or atomiser techniques may be used to generate aerosols from nanoparticles in liquid suspensions. These aerosols may be used for a subsequent

analysis using aerosol instruments (such as Scanning Mobility Particle Sizers, SMPS) based on ISO-standards as well as SI-traceable aerosol number concentrations. Furthermore, the nanoparticles can be deposited onto substrates for further analysis of size or chemistry. Industry currently has no guidance or methodology in these areas and the emerging activities to address this issue in ISO/TC229 ISO/TC24/SC4 and CEN/TC352 require support from the metrology community.

All nanoparticles have external coatings. Sometimes the coating is intentional and is required to guarantee specific performance, examples being prevention of aggregation, capping layers on quantum dots to improve photoluminescence quantum yields and reduce environmental reactivity, surface functional groups to enable biolabelling, and protein coatings in diagnostic and drug delivery applications, core-shell metallic systems (e.g. Pd@Pt) to enhance catalyst performance and fluorocarbon coatings on magnetic particles for ferrofluid applications. In other cases the coating is unintentional oxidation or contamination of the particle surface. All of these affect nanoparticle performance. Hence, understanding and controlling the surface chemistry of particles and quantifying the number of functional groups available for further reaction is fundamental to the successful formulation of products and their reliable performance.

The measurement of shell chemistries is therefore of major importance and this has long been recognised within the catalysis community where supported metal catalysts have been studied for many decades. The application of quantitative vacuum-based surface spectroscopies such as Auger Electron and X-ray Photoelectron Spectroscopy and X-ray Absorption Spectroscopies and scattering methods such as Anomalous Small Angle X-ray Scattering have been demonstrated, but all require refinement to enable industry to access the wealth of information available. In principle, the amount of material and the elemental composition of the shell can be measured using these methods as well as some information on chemical structure. Other methods may also be important. Secondary ion mass spectrometry can identify chemical species on the surface of nanoparticles, and ion scattering used to measure shell thickness, but a quantitative framework is far from established. One of the key challenges in applying these methods to nanoparticle suspensions is the preparation required to transfer the particle to a surface without introducing artefacts or sampling bias. This is a similar issue to TEM analysis and input into documentary standards on sample preparation methods, currently under discussion in ISO/TC201 and ISO/TC229, is required. To make progress in all of these areas, the provision of adequate core-shell reference materials and traceable measurements through which these may be certified is needed. For industrial applications, it is necessary to find techniques that provide surface chemical information *in-situ* and/or with easily performable assays. Currently, zeta-potential measurements are employed as a simple method of assessing particle surfaces: this is simply inadequate. Conductivity measurements or spectroscopic assays with suitable labels for common surface functional groups have been demonstrated, but comparable and validated methods are missing. Optical techniques operating in the wavelength ranges in which water is transparent, such as Raman and UV-visible spectroscopies, should be developed. Recently, it has been shown that the non-linear optical processes second harmonic generation (SHG) and sum frequency generation (SFG) can be applied to nanoparticles and are highly sensitive to surface effects, such as changes in shell chemistry and electric fields. These may offer useful quality control measurements for nanoparticle manufacturers and users if they are developed within a metrological framework and a better understanding of the physical parameters that influence their sensitivity is established.

## Objectives

Proposers should address the objectives stated below, which are based on the PRT submissions. Proposers may identify amendments to the objectives or choose to address a subset of them in order to maximise the overall impact, or address budgetary or scientific / technical constraints, but the reasons for this should be clearly stated in the proposal.

The JRP shall focus on the traceable measurement and characterisation of nanoparticle number concentrations and chemistry, including the chemistry and thickness of nanoparticle shells.

The specific objectives are

1. To develop traceable measurement and calibration protocols to measure particle number concentrations in liquid suspension to better than 10 % uncertainty for particles in the size range 1 nm to 1000 nm.
2. To develop methods to quantify the number of particles in partially agglomerated or aggregated states within a liquid suspension of otherwise monodisperse primary particles.
3. To develop standard procedures to traceably measure the chemical composition and thickness of the nanoparticle shell, both to within 10 % uncertainty.

4. To conduct an inter-laboratory study to establish best practice for industry and thereby establish laboratory-scale methods to enable valid, routine monitoring and quality control of particle concentration and surface chemistry for nanoparticle-based formulations and products.
5. To engage with industry that manufactures and or / exploits nanoparticles in order to facilitate the take up of the technology and measurement infrastructure developed by the project, to support the development of new, innovative products, thereby enhancing the competitiveness of EU industry.

Proposers shall give priority to work that meets documented industrial needs and include measures to support transfer into industry by cooperation and by standardisation. An active involvement of industrial stakeholders is expected in order to align the project with their needs – both through project steering boards and participation in the research activities.

Proposers should establish the current state of the art, and explain how their proposed project goes beyond this.

EURAMET expects the average EU Contribution for the selected JRPs to be 1.5 M€, and has defined an upper limit of 1.8 M€ for any project.

EURAMET also expects the EU Contribution to the external funded partners to not exceed 30 % of the total EU Contribution to the project. Any deviation from this must be justified.

Any industrial partners that will receive significant benefit from the results of the proposed project are expected to be unfunded partners.

## Potential Impact

Proposals must demonstrate adequate and appropriate participation/links to the “end user” community, describing how the project partners will engage with relevant communities during the project to facilitate knowledge transfer and accelerate the uptake of project outputs. Evidence of support from the “end user” community (e.g. letters of support) is also encouraged.

You should detail how your JRP results are going to:

- Address the SRT objectives and deliver solutions to the documented needs,
- Drive innovation in industrial production and facilitate new or significantly improved products through exploiting top-level metrological technology,
- Improve the competitiveness of EU industry,
- Feed into the development of urgent documentary standards through appropriate standards bodies,
- Transfer knowledge to the nanotechnology sector.

You should detail other impacts of your proposed JRP as specified in the document “Guide 4: Writing Joint Research Projects”

You should also detail how your approach to realising the objectives will further the aim of EMPIR to develop a coherent approach at the European level in the field of metrology and include the best available contributions from across the metrology community. Specifically the opportunities for:

- improvement of the efficiency of use of available resources to better meet metrological needs and to assure the traceability of national standards
- the metrology capacity of EURAMET Member States whose metrology programmes are at an early stage of development to be increased
- organisations other than NMIs and DIs to be involved in the work

## Time-scale

The project should be of up to 3 years duration.