Title: Improved traceability chain of nanoparticle size measurements

Abstract

Nanoparticles and nanofibers are being increasingly incorporated into new products with applications in health care, information and communication technologies, energy production and storage, materials science/chemical engineering, and manufacturing. However nanotechnologies and nanoparticles may expose humans and the environment to new health and sustainability risks. The EC has mandated CEN, CENELEC and ETSI to develop European standards for methods that can characterise manufactured nanomaterials. Therefore, accurate measurement methods and new reference materials are required to accurately characterise nanoparticles and to determine the size and size distribution of nanoparticles in order to support the introduction of international nanoparticle standards.

Keywords
Traceability, nanomaterial, nanoparticle, reference materials, shape, morphology, quantity, size distribution.

Background to the Metrological Challenges

New and emerging uses of nanoparticles and nanofibres include medical and pharmaceutical applications (e.g. antimicrobial coatings, drug delivery methods and scaffolds for bone growth), as well as use in conductive inks, optical sensing and power delivery. In 2015, the global market for nanofibers was estimated as 390.6 million USD, while the potential market for silver nanoparticles alone was estimated at 2.54 billion USD by 2022. Particle characterisation instrumentation also generated revenue of USD 701 million in 2014 and is estimated to grow to 1048 million USD by 2019. Therefore to support the increasing and safe use of nanomaterials it is essential that robust normative standards are introduced to facilitate comparable and traceable calibrations and measurements and as a prerequisite for new nanomaterial safety standards.

EC Mandate M/409 states '*A thriving high-tech industry is a key to Europe's economic and political viability due to its direct and indirect effect (e.g. spill-over effects). Consequently, it is of utmost importance to translate European excellence in nanosciences into safe and commercially marketable products and processes*'. In addition, EC Mandate M/461 requires CEN, CENELEC and ETSI to develop standards activities regarding nanotechnologies and nanomaterials as one of the building blocks for the "*safe, integrated and responsible*" use of nanomaterials as outlined in the EC European Strategy for Nanotechnologies.

CEN TC 352 "Nanotechnologies" is addressing the requirements of these mandates, and has formulated a list of research needs, which includes '*Measurement, simulation and visualization at the nanoscale*' and '*Methods to characterize basic morphology and purity of manufactured nanoparticles and other nanoscale entities*' for the investigation of the influence of a nano-object's shape on size measurements. However, current challenges for reliable nanoparticle size measurements include the reduction of measurement uncertainties and improvements to the comparability of results from different measurement methods, which can be as large as 100 %. This issue with comparability can be attributed to an insufficient knowledge of the dependency of specific measurement methods on nanoparticle material and shape, and how different instruments or laboratories, using the same method, treat the raw, measured output signals.

Currently there are no validated nanoparticle reference materials with non-spherical shapes or non-monodisperse size distributions and therefore spherical monodisperse reference materials are used. However relating an instrument's calibrated output signal to the complex shapes or particle agglomerations required in real world measurements using certified spherical monodisperse reference materials is problematic. This is compounded by a lack of physical material simulation models suitable for addressing the changes in instrument output signal introduced by measuring different types of material. Therefore, nanoparticle reference materials with well-defined non-spherical shapes (i.e. elongated, platelets, etc.), differing size distributions and defined nanoparticle concentrations in terms of number, volume, and mass are needed to reduce measurement uncertainties and increase the robustness of nanoparticle measurements.

ISO/TC 229 'Nanotechnologies' has recently initiated standardisation projects on the measurement of nanoparticle size and shape distribution using electron microscopy techniques such as SEM, TSEM, TEM and AFM. However, an improved understanding and better evaluation of errors is required so that particle size measurements can be used for size distributions. For example errors such as those introduced when not all particles are 'visible' or deposited on substrates during electron microscopy need to be addressed. Further to this, ensemble methods, like SAXS also require evaluation in terms of their output signal intensity and the consequent interpretation of quantity.

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 protocol.

The JRP shall focus on improving the traceability and comparability of different measurement systems and characterisation methods used to determine the size and size distribution of nanoparticles.

The specific objectives are

1. To assess the performance and establish the traceability of existing nanoparticle size and characterisation methods, such as SEM, TSEM, TEM, AFM and SAXS, in terms of their sensitivity to material, shape and quantity (number, volume or mass). This should use representative nanoparticulate materials (i.e. metals, oxides and polymers) and include an analysis of material properties and the effect of material and shape parameters on size and size distribution measurements, as well as the effect of conversion of the measured signal on the particle size distribution.
2. To develop validated nanoparticle reference materials with (i) non-spherical shapes, (ii) non-monodisperse size distributions and (iii) accurate nanoparticle concentrations. In addition to use such nanoparticle reference materials to evaluate measurement uncertainties for nanoparticle quantity determination (expressed as number, volume, mass or intensity) and establish its dependence on particle size.
3. To develop improved physical models of output signals from nanoparticle measurement systems, that accurately account for nanoparticle material, shape and quantity. The physical models should include nanoparticle material type, shape and its quantity parameters such as number, volume, and mass. The goal of the models is to improve the evaluation of nanoparticle measurement uncertainty and to compare results of the different methods.
4. To use the physical models from objective 3 to develop validated and traceable methods for the transfer of nanoparticle size from (certified) reference nanoparticles of spherical shape and monodisperse size distribution to other types of nanoparticles. This should include different nanoparticle shapes (such as elongated artefacts and platelets) as well as nanoparticles with non-monodisperse size distribution.
5. To contribute to the standards development work of the technical committees CEN TC 352 Nanotechnologies and ISO TC 229 Nanotechnologies to ensure that the outputs of the project are aligned with their needs, communicated quickly to those developing the standards and to those who will use them, and in a form that can be incorporated into the standards at the earliest opportunity.

EURAMET expects the average EU Contribution for the selected JRPs in this TP to be 1.2 M€, and has defined an upper limit of 1.5 M€ for this 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 industrial partners that will receive significant benefit from the results of the proposed project are expected to be unfunded partners.

The proposed research shall be justified by clear reference to the measurement needs within strategic documents published by the relevant Standards Developing Organisation or by a letter signed by the convenor of the respective TC/WG. EURAMET encourages proposals that include representatives from industry, regulators and standardisation bodies actively participating in the projects. The proposal must name a "Chief

Stakeholder", not a member of the consortium, but a representative of the user community that will benefit from the proposed work. The "Chief Stakeholder" should write a letter of support explaining how their organisation will make use of the outcomes from the research, be consulted regularly by the consortium during the project to ensure that the planned outcomes are still relevant, and be prepared to report to EURAMET on the benefits they have gained from the project.

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,
- 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 (JRPs)".

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.

Additional information

[1] CEN/CENELEC identified this topic as one of their priorities. Details are available at: https://msu.euramet.org/current_calls/pre_norm_2017/documents/SRT_related_CEN_priorities/cen_priority_15_2016.zip

[2] EC M/409 mandate addressed to CEN, CENELEC and ETSI for the elaboration of a programme of standards to take into account the specific properties of nanotechnology and nanomaterials (2008)

[3] EC M/461 Mandate addressed to CEN, CENELEC and ETSI for standardization activities regarding nanotechnologies and nanomaterials (2010)