European Partnership on Metrology
Call 2023 –Fundamental Metrology, Industry, Normative and Research Potential

Selected Research Topic number: **SRT-n07**
Version: 1.0

Title: Standardised measurements of surface functionalities on nanoparticles

Abstract

Engineered nanomaterials with various chemical compositions are routinely fabricated for industrial applications. Their utility and performance are largely determined by surface chemistry. Documented standard procedures to measure surface functionality are required to support industrial development, quality control and to meet regulatory requirements. The proposed research aims to develop accurate measurement methods for techniques ranging from X-Ray photoelectron spectroscopy (XPS) and quantitative nuclear magnetic resonance spectrometry (qNMR) to specific inexpensive titration methods and optical assays. It also proposes leadings international comparison studies to validate the methods, disseminate reference data and materials, and the development of key documentary standards.

Keywords

Functional groups, surface chemistry, nanotechnology, OECD, XPS, qNMR, optical assays, electrochemical titration methods, interlaboratory comparison, chemicals´ regulation REACH (2006/1907), cosmetic products regulation (2009/1223)

Background to the Metrological Challenges

Engineered nano and micro-particles are used in many applications from medical diagnostics to photovoltaics. Many of the more advanced applications utilise sophisticated nanoparticles which have complex morphology and surface chemistry. To achieve the desired result, sequential surface chemical reactions are often required to form a functional composite. Resulting surface modifications need to be accurately characterised to ensure the effectiveness of surface functionalisation. The ability to characterise the surface chemistry of nano-objects is therefore vital for quality control of nanoparticles systems to meet increasing concerns regarding their safety. Industry, regulatory agencies, and policymakers need validated traceable measurement methods and candidate reference and test materials. For example, industry must comply with various regulations, such as the chemicals´ regulation REACH (2006/1907) or cosmetic products regulation (2009/1223), depending on the use. In addition, the European Medical Agency (EMA) and the European Commission's Joint Research Centre (JRC) have expressed needs for measurement methods related to the quality and safety assessment of nanomedicines and for surface properties of nanomaterials respectively. Within ISO/TC 201, standardisation of the analysis of nanomaterials has been recognised as a high priority.

The last few years have seen the publication of documentary standards for the measurement of nanoparticle size and shape. However, surface chemistry analysis methods for nano or micro-particles are largely non-standardized. A preliminary work item (PWI 19257) in ISO/TC 229 on surface functional groups and coatings on nano-objects has been accepted but requires international interlaboratory studies to progress. The Partnership project 22HLT04 MetrINo aims to develop and validate traceable methods to measure nanoparticle physical properties, biotransformation in biological media, and methods for their identification and quantification in cells and tissues for clinical formulations. Stakeholders have expressed a need for standardised methodologies for measuring nanoparticle surface properties, including the amount, chemical composition, and homogeneity of the surface coating and reference materials but the project is not directly addressing this specific measurement issue. Previous EMPIR project 17SIP03 EsCoShell led the development of an informative ISO Technical Report 23173. This report is limited to providing information only on uniform core-shell nanoparticles which is not only a limitation for coating, but also for other surface functionalisation. It does not provide normative methodology which is required for a full standard. In addition, compensating for morphology variation is vital to ensure that such systems can be adequately measured by XPS to validate other, non-surface specific analysis techniques.

Measurement equipment and expertise for XPS and Time of Flight Secondary Ion Mass Spectrometry (ToF-SIMS) reside in NMIs, industry research centres and universities. Methods such as qNMR are increasingly used to obtain accurate measurements of total functional group concentration. However, the quantitative comparability of advanced surface-specific and simpler 'bulk like' measurements urgently need to be determined. In most industries, particularly SMEs, more affordable techniques are used, such as electrochemical titration methods and optical assays with colorimetric or fluorescence readout exploiting the large toolbox of reactive dyes for signal generation. In these cases, standards, test and reference materials for calibration are required.

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 metrology research necessary to support standardisation in surface chemical analysis of nano-objects for industrial applications focussing on the quantification of surface functionalities.

The specific objectives are

1. To develop methods for the quantification of surface functionalities and coatings on nanomaterials. This will contribute to the development of i) Preliminary Work Item (PWI) 19257 (ISO TC229) on surface functional groups and coatings on nano-objects, and (ii) PWI (IEC TC113) on characteristic functional groups by conductometry for electrotechnical systems and (iii) technical guideline in working group WNT 1.6 of Organisation for Economic Co-operation and Development (OECD): surface chemistry and coatings of nano- and micro-particle.
2. Building upon ISO TR 23173 (ISO TC201) and work of EMPIR project 17SIP03 ESCoShell, to develop a validated quantitative procedure for the measurement of thickness and composition of nanoparticle coatings and other surface functionalisation using electron spectroscopies such as XPS. This will form the basis of a full international standard.
3. Using methods and procedures developed in objectives 1 and 2, to perform international interlaboratory comparisons (ILCs) on quantification and determination of surface chemistry, under the auspices of VAMAS TWA 2 (surface chemical analysis), with different types of nano-objects (e.g., silica, iron oxide, gold and lanthanide-based) as well as polymer nanoparticles with industry-relevant surface functionalities (e.g., amine, carboxyl, and thiol groups, azide and alkyne). Methods such as XPS, ToF-SIMS, and qNMR will be combined with optical and electrochemical methods.
4. Using input from the ILCs from objective 3, to produce and disseminate test and reference materials, as well as reference data and methods, to the nanotechnology community to underpin the development of quality control methods in nanomaterial production. The reference materials will be used to initiate future BIPM CCQM pilot studies, where feasible.
5. To contribute to the standards development work of the technical committees ISO TC 229, IEC TC113 and ISO TC 201 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.

The proposed research shall be justified by clear reference to the measurement needs within strategic documents published by the relevant Regulatory body or 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.

Proposers should establish the current state of the art and explain how their proposed research goes beyond this. In particular, proposers should outline the achievements of the EMPIR project 17SIP03 ESCoShell and Partnership project 22HLT04 MetroINo and how their proposal will build on those.

EURAMET expects the average EU Contribution for the selected JRPs in this TP to be 1.0 M€ and has defined an upper limit of 1.3 M€ for this project.

EURAMET also expects the EU Contribution to the external funded beneficiaries to not exceed 30 % of the total EU Contribution across all selected projects in this TP.

Any industrial beneficiaries that will receive significant benefit from the results of the proposed project are expected to be beneficiaries without receiving funding or associated 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
- Feed into the development of urgent documentary standards through appropriate standards bodies,
- Facilitate improved industrial capability or improved quality of life for European citizens in terms of personal health, protection of the environment and the climate, or energy security,
- 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 the Partnership 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.