Title: Establishing traceable concentration measurements of particles for a more sustainable industry

Abstract

Transitioning to a sustainable industry requires advanced materials for priority sectors like energy, semiconductors, health and personal care. Advanced complex particles defy accurate measuring by current methods, therefore there is a need for updating current standards to include traceable evaluation of the number concentration of complex particles to address industry regulations. This requires development of accurate, harmonised methods for measuring the particle density and refractive index required by established industrial practices for number concentration determination. Proposals addressing this SRT should deliver methods and documentary standards that enable regulatory compliance and commercialisation of particle-based products of value to sustainable industry.

Keywords

Advanced materials, Nanoparticles, Particle density, Particle number concentration, Refractive index (RI).

Background to the Metrological Challenges

Supporting the green transition in key areas is one of the objectives of the NDICI-Global Europe 'Global Challenges' thematic programme [1] (Neighbourhood, Development and International Cooperation Instrument) aligning with the United Nations 2030 Agenda for Sustainable Development [2]. Advanced materials play a crucial role in achieving these goals for transitioning the industry to a green and circular economy. The EU Industrial Strategy offers an in-depth analysis of 6 strategic areas where the EU has dependencies [3]. Four of these strategic areas, namely batteries, active pharmaceutical ingredients, hydrogen, and semiconductors require technology which is based on advanced materials.

The Advanced Materials 2030 Initiative further emphasises this need in their roadmap [4]. It outlines that advanced materials are required to address sustainability concerns and improve production processes while ensuring safety standards for these materials, which often have complex compositions. Many of these needed advanced materials are particulate in nature.

Therefore, there is a need of the development of robust measurement methods to accurately determine particle concentration for the whole life cycle of these materials from production over usage to disposal and possibly unwanted leakage into the environment. This is corroborated by the CCQM Strategy Document 2021-2030, which requests extending particle metrology to "improve measurement methods and uncertainties of particle mass, size and number concentration measurements and the characterisation of regulated components" as well as "reliable measurements for emerging food contaminants such as [...] microplastics and nano particles". [5]

In line with these needs, the EMN for Pollution Monitoring (POLMO) prompts to address urgent concerns across its Air and Water sections, with a focus on key challenges related to pollutants of emerging concern [6]. High priority is given to the number concentration of ultrafine particles in air and the corresponding number size distribution. In the Water section, POLMO prioritises tackling microplastics pollution with a focus on harmonising limit-of-detection/quantification methodologies to enhance the monitoring and management of these contaminants in aquatic environments.

For nanoform materials that are not trace pollutants but used in high concentration in technical and scientific applications, ECHA (European Chemical Agency) requires characterisation per "Guidance on information requirements and chemical safety assessment” including number-based particle size distribution [7]. Regulations on safety for particulate materials also differ across the world, which makes it only more important to have reliable measurement methods [8, 9].

The need for number concentration and number-based size distribution measurements also arises for particles of biological origin such as viruses, vaccines, and extracellular vesicles. The number concentration in a certain size range is relevant for clinical diagnosis and pharmacological formulations. In these medical products and body fluids, different types of particles can co-exist (e.g., extracellular vesicles and lipoproteins), each having its own material properties and size. Number concentration is also an important parameter in pharmaceutical formulations, directly influencing drug encapsulation per particle and their dosage to therapeutic targets. The EMN for Advanced Manufacturing therefore requests research to support regulatory requirements related to nanomaterials under REACH, on medical devices (Regulation (EU) 2017/745) and in-vitro diagnostic devices (Regulation (EU) 2017/746).

There is an urgent demand for innovative and robust measurement methods to accurately determine particle concentration across various industries and sectors as part of the global transition towards a sustainable green economy. To fully address this need, the development of traceable certified reference materials with specified properties such as size, density, and complex refractive index is essential in order to advance research and regulatory frameworks related to nanomaterials under REACH and for medical devices and diagnostic applications.

Although significant research effort has been dedicated to the development, advancing and standardisation of number-based concentration measurements, to date, the applicability of these methods has been demonstrated only for idealised monodispersed, spherical monomodal, and to some extent bimodal, materials. Furthermore, although the applicability of various ensemble methods to number-based particle concentration determination has been demonstrated using these idealised particle systems, key input parameters, such as particle density and the RI have so far been sourced from literature. This is because there is a lack of validated methods for the measurements of these particle attributes, which represents a stumbling block to the extension of developed methods to more complex industrial particles.

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 proposal shall focus on metrology research necessary to support standardisation in the traceable measurement and characterisation of particles for a more sustainable industry.

The specific objectives are:

1. To develop relevant (for health and personal care, semiconductor or energy materials, or represent typical environmental pollutants such as nanoplastics) representative test materials (RTMs) for number concentration measurements of nano- and sub-micrometre particles. The RTMs shall cover relevant ranges of density, size and concentration (low for pollutants, high for industrial particles) and come with indications of refractive index, size, and density.
2. To verify the performance of established references and laboratory methods for measurements of the number concentration of relevant RTMs and to develop new, material-specific sample preparation protocols for, e.g., imaging methods. To run an interlaboratory comparison to compare the performance of particle (between 1 nm and 1000 nm) counting methods and ensemble methods (e.g., SMLS, SAXS, MADLS, DCS, UV-Vis, Raman spectroscopy).
3. To develop traceable methods for particle material characterisation, aiming to reduce the uncertainty of concentration measurements by ensemble methods, and to define uncertainty requirements for density and refractive index as input parameters for number concentration measurements. For density measurements, to consider a selection of methods such as TGA, CLS, XRD, multi-velocity CLS and dry mass measurements. For refractive index measurements, to consider ensemble and single-particle methods such as FCM, UV-VIS, FFF-RI, light scattering, and laser diffraction.
4. To validate modelling of material parameters in the measurement processes and develop a roadmap for generating traceability and standardisation of particle refractive index measurements.
5. To collaborate with the technical committees CEN/TC 352, ISO/TC 24/SC 4 and ISO/TC 229 and ISO/TC 276 and the users of the standards they develop to ensure that the outputs of the project are aligned with their needs, including the revision of standards ISO TS/24672 on particle concentration

measurements, ISO 18747 on density measurements, ISO TS/21357 on SMLS, and NWIP ISO TS 4807 on reference materials and recommendations for incorporation of this information into future 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 projects 14IND12 Innanopart, 18SIP01 ISOCONCur, 17NRM04 nPSize and Metrology Partnership projects 21GRD07 PlasticTrace and 22HLT04 MetrINo and how their proposal will build on those.

Proposers should note that the programme funds the activity of researchers to develop the capability, not the required infrastructure and capital equipment, which must be provided from other sources.

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 proposal.

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 proposal’s 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 advanced materials (batteries, active pharmaceutical ingredients, hydrogen, and semiconductors) industry 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 Metrology 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.

Timescale

The project should be of up to 3 years duration.

Additional information

The links provided in this section are only correct at the time of publication up until the end of the Call year.

The references below were provided by PRT submitters; proposers should therefore establish the relevance of any references.

[1] *'Global Challenges' thematic programme, NDICI Global Europe* https://knowledge4policy.ec.europa.eu/publication/ndici-global-europe-%E2%80%98global-challenges%E2%80%99-thematic-programme-multi-annual-indicative_en

[2] *UN 2030 Agenda on Sustainable Development* https://sdgs.un.org/2030agenda

[3] *EU Industrial Strategy* https://commission.europa.eu/strategy-and-policy/priorities-2019-2024/europe-fit-digital-age/european-industrial-strategy/depth-reviews-strategic-areas-europes-interests_en

[4] *Materials 2030 Roadmap, AMi2030*, https://www.ami2030.eu/roadmap/

[5] *CCQM Strategy Document 2021-2030* https://www.bipm.org/documents/20126/2071059/CCQM+Strategy.pdf/31283069-94f4-f2c7-bbfc-7d652c9b3de8

[6] *EPM Green Deal Call 2024 Orientation, EMN for Pollution Monitoring (POLMO)* https://www.metpart.eu/component/edocman/call-2024-emn-pm/download.html?Itemid=0

[7] *ECHA-22-G-02-EN Guidance on information requirements and chemical safety assessment* Appendix R7-1 for nanomaterials applicable to Chapter R7a DOI: 10.2823/496606, 2022

[8] *How nanoparticles are counted in global regulatory nanomaterial definitions,* https://www.nature.com/articles/s41565-023-01578-x

[9] https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32022H0614(01)