European Metrology Programme for Innovation and Research

Delivering Impact

Measuring nanoparticle exposure

Nanoparticles are a subject of intense scientific and technological interest in many industries, from medicine to electronics. The global annual nanomaterials market is already worth about €20 billion, exploiting unusual properties of these tiny, highly functional materials. Some nanoparticles may be toxic but there's no way to reliably measure exposure. Lack of traceable methods to measure dosage reduced confidence in instrumentation, so impeded the development of new applications.

Europe's National Measurement Institutes working together

The European Metrology Programme for Innovation and Research (EMPIR) has been developed as part of Horizon 2020, the EU Framework Programme for Research and Innovation. EMPIR funding is drawn from 28 participating EURAMET member states to support collaborative research between Measurement Institutes, academia and industry both within and outside Europe to address key metrology challenges and ensure that measurement science meets the future.

Challenge

Nanotechnology is a promising enabling technology, expected to give rise to new solutions and markets in many areas of research and industry. Nanoparticles are highly functional particles ranging in size from between 1 and 100 nanometres, with properties largely determined by a reactive outer layer. Already a €20BN global industry, applications include quantum dots in TV displays and delivery systems for cancer drugs.

While not necessarily hazardous, the unusual properties of nanoparticles make it difficult to predict any toxic effects. The EU Commission is reviewing its definition of what constitutes a nanomaterial, that currently solely considers particle size. Particle number concentration, a measure of the total number of particles per unit volume, is more relevant to dosage, such as in nanomedicine or for exposure to aquatic organisms in drinking water. However, no traceable methods existed to measure this number. As nanoparticles tend to clump together, which affects concentration measurements, a lack of understanding of dispersion properties added to the uncertainty.

The most common measurement technique, dynamic light scattering, offered, at best, errors of a factor of two for concentration. The result was a lack of reproducibility for research outputs, limiting the potential for industrial innovation. There was, therefore, a pressing need for standardisation, and for nanoparticle reference materials with known concentration for instrument calibration.

Solution

The EMPIR project *Metrology for innovative nanoparticles* assessed four candidate particle types for suitability as reference materials and benchmarked seven measurement techniques for particle number concentration.

Two methods were selected: small-angle X-ray scattering, and single-particle inductively coupled plasma mass spectrometry. Combined with a high-resolution method to distinguish single and aggregated particles, these methods enabled measurements of concentration accurate to within 10%. Citrate stabilised gold 30 nanometre nanoparticles were judged suitable for use as a reference material.

The developed standard reference material was a world-first for providing metrological traceability for nanoparticle products, validating analytical measurement methods, and calibrating instruments.

Impact

Malvern Panalytical, a leading provider of scientific instrumentation, recognised that particle sizing instruments using DLS, although quick and user-friendly, were not capable of providing accurate measurements of particle concentration.

During the project, the company approached the consortium to validate the performance of a prototype of its Zetasizer Ultra. This device applied two types of light scattering technology: DLS and electrophoretic light scattering. With no validated reference material for particle concentration available, calibrations were being performed using its unvalidated sample, that could not deliver total confidence in the accuracy of the resulting data.

The reference material provided by the consortium enabled Malvern Panalytical to have confidence in the capability of the Zetasizer Ultra for measuring particle concentration. This enabled it to promote multi-angle dynamic light scattering particle concentration measurement as a feature from product launch in 2018. The company gained access to sales opportunities in new application areas, for which it acknowledges the significance of the metrology solutions developed in the project.

Traceable measurement and calibration protocols for particle number concentration measurements will enable companies to develop methods and measurement instrumentation to meet evolving EU regulatory requirements, and help scientists and industry develop innovative applications. Ultimately, these developments will help ensure the safety of nanomaterial-containing products for consumers.

Metrology for innovative nanoparticles

The project developed two methods to traceably measure and calibrate particle number concentration, by applying small-angle X-ray scattering and single-particle inductively coupled plasma mass spectrometry, both to within 10% accuracy. To confirm the measurements, protocols were developed to distinguish between single and clumped-together particles.

Procedures were developed to determine nanoparticle concentration and for nanoparticle surface chemical analysis. These protocols were validated in major inter-laboratory studies, showing the methods to be clear and consistent.

The procedures were developed into good practice guidance and are applied in the follow-on ISOCONCur project as an International Organization for Standardization technical report. In due course, standards and regulatory compliance will further support acceptance, enabling the development of innovative nanoparticle-based products.

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