Report of the Joint CCQM-IAWG/SAWG Task Group on Particle Metrology

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ABSTRACT

This report details the recommendations of the joint CCQM-IAWG/SAWG Task Group on Particle Metrology (CCQM-IAWG-SAWG-TG-PARTICLE) on the activities that IAWG and SAWG should undertake in the next decade. The Task Group was established in November 2023 and met quarterly over the next two years to discuss the state of the art and gaps in particle metrology that underpin industrial prosperity and quality of life.

CONTENTS

GLOSSARY AND ABBREVIATIONS

Useful definitions

From ISO 80004-1:2023: *Nanotechnologies – Vocabulary — Part 1: Core vocabulary*

Particle: minute piece of matter with defined physical boundaries.

Nanomaterial: material with any external dimension in the nanoscale or having internal structure or surface structure in the nanoscale**.**

Nanoscale: length range approximately from 1 nm to 100 nm.

Nanoparticle: nano-object with all external dimensions in the nanoscale.

Nano-object: discrete piece of material with one, two or three external dimensions in the nanoscale.

Nanomaterial: material with any external dimension in the nanoscale or having internal structure or surface structure in the nanoscale.

Abbreviations:

BIPM: International Bureau of Weights and Measures

CCEM: Consultative Committee for Electricity and Magnetism

CCL: Consultative Committee for Length

CCQM: Consultative Committee for Amount of Substance: Metrology in Chemistry and Biology

CCQM TG-FOOD: CCQM Task Group on Food Measurement

CCQM TG-GDS: CCQM Task Group on Gene Delivery Systems

CCQM TG-NMMS: CCQM Task Group on Nano- and Microplastics Measurements and Standards

CRM: certified reference material

DI: Designated Institute

GAWG: CCQM Working Group on Gas Analysis

IAWG: CCQM Working Group on Inorganic Analysis

NMI: National Metrology Institute

NAWG: Working Group on Nucleic Acid Analysis

OAWG: Working Group on Organic Analysis

PAWG: Working Group on Protein Analysis

RM: Reference Material

SAWG: Working Group on Surface Analysis

SAXS: Small angle X-ray scattering

SI: The International System of Units

spICP-MS: single-particle inductively coupled plasma mass spectrometry

VAMAS: Versailles Project on Advanced Materials and Standards

XPS: X-ray photoelectron spectroscopy

EXECUTIVE SUMMARY

The Joint CCQM-IAWG/SAWG Task Group on Particle Metrology was established in 2023 to define the metrological activities needed over the next decade to support innovation, regulation and quality assurance for particle-based materials. The Task Group reviewed industrial and regulatory drivers, surveyed current measurement capabilities, assessed gaps in reference materials and traceable measurement methods for different types of measurands, and considered the measurement challenges associated with increasingly complex particle systems used across healthcare, energy, manufacturing and environmental monitoring.

Particle-based products now span wide dimensional, chemical and structural ranges and play a critical role in sectors such as nanomedicine, advanced materials, catalysis, semiconductors, food and cosmetics. In parallel, global regulatory and sustainability agendas are creating strong demand for robust, traceable measurement infrastructure. Key drivers identified include the need for improved characterisation of complex particle designs, strengthened regulatory compliance, protection of human and environmental health, and the transition to more sustainable manufacturing processes with reduced waste and solvent use.

The Task Group found significant progress in CCQM activities, including key comparisons for particle number concentration using gold nanoparticles. However, the current global metrology system lacks sufficient certified reference materials, validated methods and harmonised approaches to meet stakeholder needs across real-world matrices and heterogeneous particle types. Gaps were identified in areas such as polydisperse and agglomerated systems, coatings and surface functionalities, particles embedded in complex matrices, and particles containing multiple chemistries. Several critically important measurands—particle refractive index, particle density and surface charge—have no established SI-traceable methods, despite underpinning widely used industrial techniques.

The report sets out a roadmap of priority activities for CCQM, including pilot studies on particles in complex matrices, surface functional group quantification, and multi-chemistry core–shell systems. It also recommends initiating metrology development for refractive index, density and surface charge. Strengthened cooperation between CCQM working groups, improved engagement with regulators and industry, and expanded mechanisms for stakeholder participation in comparisons are essential to ensure relevance and accelerate impact.

Delivering these recommendations will enable a coherent, coordinated particle metrology framework that supports global regulatory harmonisation, de-risks industrial innovation, and provides the traceability required for emerging particle-based technologies.

1 INTRODUCTION

A CCQM virtual workshop on Particle metrology was held in October 2022, chaired by Michael Winchester (NIST). One of the recommendations that emerged from the workshop was the formation of a number of task groups within CCQM that could examine present and future needs for particle metrology.

The Joint CCQM-IAWG/SAWG Task Group on Particle Metrology (CCQM-IAWG-SAWG-TG-PARTICLE) task group was created in October 2023, with Caterina Minelli (NPL) as chair, and with members from both IAWG and SAWG (see section 1.2). The terms of reference were:

To identify activities that the IAWG and SAWG should undertake with respect to particle metrology over the next ten years, including pilot studies, key comparisons, and cooperative research projects. To accomplish this, the TG will:

- *Examine the outcomes of the CCQM Workshop on Particle Metrology held 25-27 October 2022*
- *Liaise with external stakeholders to understand better the important needs and gaps in particle metrology that can be addressed by the IAWG and SAWG*
- *Liaise with the CCL WG-N to leverage knowledge and identify opportunities for cooperation between (nano)dimensional, chemical and biological activities with respect to particle metrology.*

The findings of this TG, including actionable proposals, will be delivered in this written report within 24 months.

1.1 METHOD.

The task group kicked off on 23rd November 2023 and met quarterly in online meetings during the following two years. The task group reviewed the industrial and regulatory needs for particle measurements, metrology gaps, critical stakeholders, relevant networks, projects and publications (see Appendix). This report summarises the outcomes of this review and provides some recommendations on activities that the IAWG and SAWG should undertake with respect to particle metrology over the next ten years, including pilot studies, key comparisons, and cooperative research projects.

1.2 TASK GROUP MEMBERS.

Table 1. members of the Joint CCQM-IAWG/SAWG Task Group on Particle Metrology, along with their affiliation and working group of origin.

Name	Affiliation	WG
Alex Shard	NPL (UK)	SAWG
Andrew Yacoot	NPL (UK)	CCL-WG-N
Antonio Salas	CENAM (Mexico)	IAWG
Caterina Minelli	NPL (UK)	SAWG
Chao Jingbo	NIM (China)	IAWG
Harald Bresch	BAM (Germany)	IAWG
Heidi Goenaga-Infante	LGC (UK)	IAWG
Jariya Buajarern	NIMT (Thailand)	SAWG/CCL-WG-N
Johanna Noireaux	LNE (France)	IAWG
Katherine Cardenas	INM (Colombia)	SAWG
Jorg Radnik	BAM (Germany)	SAWG
Juliana Serna Saiz	INM (Colombia)	SAWG

Maribel Moreno	INM (Colombia)	SAWG
Christhian Paredes	INM (Colombia)	SAWG
Lingling Ren	NIM (China)	SAWG
Michael Krumrey	PTB (Germany)	SAWG
Narine Oganyan	VNIIFTRI (Russia)	IAWG/SAWG
Norma González	CENAM (Mexico)	SAWG
Ute Resch-Genger	BAM (Germany)	IAWG
Victoria Coleman	NMIA (Australia)	SAWG, CCL chair
Yalizaveta Tarasenko	SE "Ukrmetrteststandard" (Ukraine)	IAWG
Yadira Guadalupe Maldonado	CENAM (Mexico)	IAWG

2 SCOPE OF THE REPORT

This report contains information and recommendations on metrology activities pertinent to:

- particles of high industrial value, in sectors including energy, health, food and cosmetics;
- particles that are present in the environment, because of human activity, with the exclusion of particles suspended in different gases but including air-based measurement-techniques where required;
- particles that are present in living organisms and the environment as a result of the degradation process of materials.

It should be noted that the activities of this task group are synergistic to those of other CCQM task groups, including:

- the CCQM-GAWG Task Group on Aerosol Metrology
- the CCQM Task Group on Nano- and Microplastics Measurements and Standards
- the CCQM Task Group on Food Measurement

Liaisons with these task groups were established early in the lifetime of the Task Group on Particle Metrology and some of their views and contributions are included in this report.

3 CCQM WORKSHOP ON PARTICLE METROLOGY

3.1 THE WORKSHOP.

The virtual CCQM Workshop on Particle Metrology, chaired by Michael Winchester (NIST), took place on 25th-27th October 2022. The workshop was organised in two plenary sections at the beginning and the end of the workshop and three parallel breakout groups on:

- Particles suspended in air or other gases (report);
- Particles suspended in water or other liquids (report);
- Particles in biological materials and pharmaceuticals (report).

For each of the three days, there were approximately 130 attendees, including those giving presentations and leading discussions, with a good mix of representation from the CCQM and stakeholders.

The workshop outputted three action items, of which the one relevant to this Task Group is:

Create a task group within the CCQM to foster communication between communities, consider interlaboratory comparisons, harmonize protocols, and provide sample preparation guidance, among other tasks. Engagement with VAMAS should be useful. Details regarding measurement gaps and other topics are found in CCQM-WS/2022-20 (Particles in Liquids –

Report from Breakout Group 2) on the workshop website. Because most of the CCQM activity for particles suspended in liquids will likely remain within the Inorganic Analysis Working Group (IAWG) and the Surface Analysis Working Group (SAWG), it is recommended that this task group be set up as a joint IAWG/SAWG task group. If other CCQM working groups need to become involved, adjustments can be made.

Outputs from discussions during the workshop have been used for the preparation of this report and integrated in the following sections.

4 FINDINGS OF THE TASK GROUP

4.1 DRIVERS.

Industrial innovation: particle-based products are ubiquitous across the health, energy, materials sectors. They cover multiple length-scales and are increasing in chemical and structural complexity. Bulk and surface chemical properties are critical to integration and performance of these products, which drives the need for robust metrology tools underpinning their development, manufacturing and deployment.

Examples: complex medicines, composed of lipid/polymer carrier of synthetic/biological therapeutics, viral vectors, cells, quantum materials (e.g. nanodiamonds), particle catalysts.

Regulatory compliance: effective regulation requires robust reference materials and standardised methods for particles (incidental or engineered) to ensure safety, streamline compliance and derisk innovation. Regulatory needs drive metrology innovation, push sensitivity requirements and inform on priorities.

Examples: particle surface functionalities, distribution and quantification of particle loading, number concentration, chemical impurity profile.

Human and environmental health: product use causes incidental release of particles. Human safety and environmental preservation drive the development of metrology capability for polydisperse samples in complex matrices.

Examples: nano- and micro-plastics in food and environment, metal-oxide particles in sun-cream formulations, silica particles in semiconductor plant wastewaters.

Resilience and sustainability: the needs for preserving limited environmental resources and reduce carbon footprint of human activity impose a rethinking of the materials, processes and analytical methods adopted by industry and drive technological innovation for reducing waste, increasing efficiency in energy use and improving materials' circularity. This impacts the way particle-based products are manufactured and measured and related metrology needs to evolve accordingly.

Examples: in/on-line analytics for continuous manufacturing, non-destructive analytics for reducing waste, miniaturised analytics to minimise the use of solvents.

4.2 REFERENCE MATRIALS AND MEASURANDS

4.2.1 State of the art

In the context of particle measurements and development of particle-based products, reference materials serve different purposes:

- Traceable calibration and verification of measurement instruments.
- Development and validation of preparative and measurement methods.
- Demonstrating regulatory compliance.

- Benchmarking capability performance.

A useful review of the state of the art of nanoparticle reference materials has been recently compiled by the Bundesanstalt für Materialforschung und -prüfung (BAM) and the National Research Council Canada [Abram, S. L.; et al. *Analytical and Bioanalytical Chemistry* 2025, 417 (12), 2405-2425].

Relevant pilot and key comparisons that members of SAWG and IAWG have participated in are reported in Table 2. We note these include pilot studies led by working groups across CCQM and particles spanning in size from the nanometre to the micrometre range.

Particle studies led by IAWG have focussed on the measurand of number concentration and have used gold nanoparticles as model systems. This includes the noteworthy milestone in 2022 of a CCQM key comparison for particle number concentration of 60 nm spherical gold particles.

Table 2 Relevant comparison studies that members of SAWG and IAWG have participated in.

Lead WG	Project	Year	Particle material	Measurand(s)
IAWG	P194	2018	30 nm spherical gold	Number concentration
IAWG	K166/P210	2022	60 nm spherical gold	Number concentration
CAWG	P222	2024	5 µm polystyrene	Number concentration
NAWG	P224	2025	Lipid nanoparticles with encapsulated RNA	Size, size distribution Number concentration

4.2.2 Gaps

It is acknowledged that the development of certified reference materials (CRMs) is a lengthy process and there are currently not enough CRMs available to allow traceability across all the required measurement applications pertinent to CCQM.

Efforts for development of new certified reference materials should therefore prioritise current gaps in traceability requirements and areas of significant social, environmental and industrial impact. Because particle products are widely spread across materials and applications, it is recognised that there are significant synergies across working parties in CCQM.

Below are some guiding principles for the development of new reference materials:

1. Reference materials representative of real-world particles:

   Available reference materials tend to be monodisperse, chemically simple and stable. These properties are often not met by real-world products, which exhibit complex – and potentially unknown – chemical compositions and structures, heterogeneities in geometries (e.g. due to manufacture or caused by agglomeration) and instability under certain conditions, e.g. dilution. As a result, ideal reference materials may not provide a representative validation or verification of preparative and measurement methods.

   There is a need for methods and guidance to handle agglomeration and polydispersity, including the development of suitable metrics, standard dispersants and preparative methods.

2. Reference materials for multiple methods and measurands:

“Particles” include vastly diverse types of materials and products with dimensions spanning from the nanometre to the micrometre range, concentrations varying over order of magnitudes and compositions including a variety of chemistries.

There is no single measurement method that can be applied across the range of dimensions, concentrations and chemistries required by stakeholders. There is a need to develop reference materials and methods with accurately assigned physical and chemical attributes that will bring consistency across these ranges and between different measurement methods.

Product properties (related to physical, chemical or biological measurands) critical to performance are often multiple and/or unknown. There is a need to develop relevant traceable reference materials for multiple measurands to simplify method validation/verification in industry and reduce the costs of developing and maintaining certified reference materials for NMIs.

For some particle products, especially in biology (e.g. viruses, drug carriers, etc), classification based on integrity, “load” or surface functional groups is essential when “counting”. There is a need to develop correlative approaches that enable consistent classification and measurements, for example using high resolution imaging and single particle methods.

3. Expanded portfolio of materials and measurands:

The main particle-related measurands CCQM IAWG and SAWG are concerned with are number concentration, amount of materials per particle (which relates to size for techniques such as spICP-MS), and particle composition, intended both in terms of bulk and surface composition (Table 3). IAWG and SAWG particle activities have so far involved relatively monodisperse mono-elemental spherical particles (gold) in simple matrix (water). There is a need to expand the **range of materials and matrixes** to enable responding to current legislations and industrial challenges. These include the measurement of particles in product and environmental matrixes.

Surface coatings and surface functionalities are critical to control and direct particles’ behaviour and integration in complex systems. The need for regulatory compliance and quality control requires increasingly accurate measurement of these coatings. Examples include targeting biomolecules at the surface of therapeutics, whose number “per particle” need to be known at both population (average) and single particle level, the latter to avoid untargeted and therefore potentially toxic delivery. There is a need to develop measurement methods that can access this chemical information. In parallel, there is a need to support the development of quantitative methods that can be easily implemented by industrial and other end user laboratories. Among these, for example, optical measurements are well suited for screening, on-line and rapid measurements, but require robust calibration strategies for quantitative measurements.

The increasing complexity of particle-based products imposes the need for methods capable to measure **multiple chemistries** within particles. This is needed also to address unknown chemistries arising from contaminants or adventitious substances. A strategy is needed to ensure many chemical elements are addressed during measurements, as opposed to selected ones. This is significant when measurands are derived from mass measurements of detected elements (e.g. particle volume in spICP-MS). Cooperation with CCL and dimensional experts is needed to localise these chemistries within the particles.

Three measurands for which no established traceable methods currently exist were identified of metrological importance for CCQM and the particle community.

a. *Particle refractive index*: this measurand underpins the ability to accurately measure other particle properties by optical methods, most notably particle number concentration by multiangle dynamic light scattering and size by laser diffraction. Both these methods are standardised and well adopted by industry. Particle refractive index also relates to chemical information, including elemental composition and loading in particle carriers.
b. *Surface charge*: this measurand provides information on particle stability and is linked to surface functionalities and is suitable for industrial implementation in product quality control and process quality assurance. Particle surface charge is typically measured by assessing particle mobility in electrical fields. This requires cooperation across consultative committees, primarily CCL and CCEM.
c. *Particle density*: this measurand relates to particle chemical composition and underpins measurement of size and concentration by other methods, e.g. sedimentation-based and small angle X-ray scattering. This is most likely accessed through a combination of mass and dimensional measurements.

4. Metrology infrastructure supporting a sustainable shift in industry.

Governments and industry are under increasing pressure to reduce emissions caused by human activity and preserve natural resources. As a result of this, industry and regulators are supporting a shift to manufacturing approaches that reduce the use of solvents, reduce waste, and avoid the use of materials with limited supply, such as helium.

As part of this approach, industry and regulators are encouraging a shift in the quality infrastructure towards process **miniaturisation** and **in/on-line measurements**. Both of these paradigms have associated analytical challenges, for example in terms of limited sample volume, sample/instrument interface and throughput.

There is a need to develop the metrology tools that support a more sustainable industrial quality framework. For example, improving the sensitivity of methods and developing non-destructive methods. The latter includes optical methods like Raman spectroscopy, for which initial normative activities are ongoing in SAWG.

Table 3 Map of measurands of interest against particle types and their industrial applications. Green = demonstrated; Yellow = some activity; red = gap.

Particle type → Measurand ↓	Metal / elemental	Oxides / simple compounds	Organic (related to OAWG, NAWG, TG-NMMS, TG-FOOD and TG-GDS)	Biological (related to CAWG, PAWG, NAWG and TG-GDS)
Number concentration in water	**CRM:** gold nanoparticles **Studies**: P194 (gold), K166/P210 (gold) **Gap**: materials other than gold, polydispersed particles.	**NEED: semiconductor particles in wastewater**	**Studies**: P222 (polystyrene), P244 (lipid nanoparticles) **NEED: manufacturing and compliance of nanotherapeutics**	**NEED: virus counting, cell counting**
Number concentration in matrixes (e.g. food, body, environmental)	***Identified IAWG/SAWG priority***. *It requires the development of reference matrixes.* **NEED: composite materials; catalysts; regulatory compliance (e.g. nano-definition); health effects of accidental particles**	**NEED: composite materials; regulatory compliance (e.g. nano-definition); health effects of accidental particles in body**	**NEED: nano- and micro- plastics in food, biological and environmental matrices**	**NEED: pollen concentration in environmental sampling; cell counting in bioreactors**
Amount of material per particle (related to size)			**NEED: intra-particle variability of loading or surface functionalities**	**NEED: viral integrity and full/empty ratio**
Particle composition – bulk	**NEED: catalyst composition;**	***Identified IAWG/SAWG priority*** **NEED: catalyst composition; particle loading, e.g. for drug delivery**	**NEED: particle loading, e.g. for drug delivery, pharmaceutical powders**	
Particle composition – surface coatings	***Identified IAWG/SAWG priority*** **NEED: heterogeneous, catalysis; nanodiamond performance for communication and biosensing; control of particle targeting, e.g. for biosensors, contrast enhancers and therapeutics**	***Identified IAWG/SAWG priority*** **NEED: heterogeneous, catalysis; surface oxidation; control of particle targeting, e.g. for contrast- and radio-enhancers**	**NEED: control of particle targeting, e.g. for biosensors and therapeutics**	**NEED: control of cell engineering**
Industrial sector	**Medical** (e.g. biosensors and pharmaceutical); energy (e.g. catalysis); **quantum communications** (e.g. nanodiamonds); **cosmetics** (e.g. carbon black); **consumer products** (e.g. antibacterial silver).	**Medical** (radiotherapy enhancers); **cosmetics** (e.g. suncreams); **food additives**; **IT** (e.g. semiconductors); **electronics** (quantum dots).	**Medical** (e.g. biosensors and complex therapeutics); **environmental** (micro- and nano-plastics).	**Pharmaceutical** (e.g. cell & gene therapy); **environmental** (e.g. pollen, bacteria, other organisms); **industrial manufacturing** (e.g. engineering biology).

4.3 RECOMMENDATIONS

1. Based on the drivers, state of the art and gaps identified in this work, the CCQM studies described in Table 4 are recommended as priorities:

Table 4 Roadmap for IAWG/SAWG activities

#	RMs and CCQM study	Short term (1-4 years)	Medium term (5-7 years)	Long term (8-10 years)
1	Particles in a range of different matrixes (oil, food, biological, model tissue systems): particle number/mass concentration, mass per particles, protein corona. It requires the development of reference matrixes.	Pilot study in liquid matrix(es)		Pilot study in solid matrix(es)
2	Particle surface functionalities: identification and quantification of surface chemical groups (e.g. amount of amine functionalities per particle)	Pilot study for qNMR, XPS and potentially ToF-SIMS methods	Pilot study for optical methods (e.g. fluorescence)	
3	Particles with multiple chemistries, e.g. core/shell: average particle composition	Pilot study on inorganic core/shell particles (e.g. by spICPMS and SAXS). Pilot study on core/shell particles with inorganic core and organic coatings (e.g. by XPS)		Pilot study on mass concentration for organic particles (e.g. Raman-based).

2. Initiate activities to start developing capability for new measurands, specifically for particle refractive index, particle density, and surface charge.

3. Set up a Particle Metrology Task Group under CCQM to enable full synergy between different working and task groups and efficient use and planning of institutes' resources.

4. Improve communication and interaction between CCQM and stakeholders from industry and regulatory bodies:
    a. Develop framework to sustain consultation, dissemination of knowledge and interactions.
    b. Enhance mechanisms for participation of external stakeholders in CCQM-related activities, e.g. parallel intercomparisons, like CCQM pilot study P194 and VAMAS TWA 34 P10 for number concentration measurements of colloidal gold, which were run in parallel utilising the same materials.
    c. Exploit CCQM work to underpin harmonisation of documentary standards, regulatory guidance and reference materials to streamline regulatory compliance and simplify the work of industry.
    d. Run effective engagement with stakeholders, to timely develop metrology outputs relevant to a fast-paced industry, e.g. through targeted CCQM workshops.

4.4 NEXT STEPS

This report will be delivered to Dr Michael Winchester in March 2026 and presented to CCQM IAWG and SAWG in April 2026.

5 APPENDIX - BACKGROUND INFORMATION

5.1 RELEVANT REGULATION AND LITTERATURE.

5.1.1 General OECD guidance.

Series on Safety of Manufactured Nanomaterials (NM)

- Test No. 125: Nanomaterial Particle Size and Size Distribution of Nanomaterials
- Test No. 124: Determination of the Volume Specific Surface Area of Manufactured Nanomaterials
- Test No. 126: Determination of the Hydrophobicity Index of Nanomaterials Through an Affinity Measurement
- Test No. 318: Dispersion Stability of Nanomaterials in Simulated Environmental Media

5.1.2 Useful reading:

- Bartczak et al. (2025). SI-traceable characterisation of the first reference material for nanoparticle number concentration in suspension to support regulatory compliance. Analytical and Bioanalytical Chemistry 417, 2655.
- Abram et al. (2025). *Nanoscale reference and test materials for the validation of characterization methods for engineered nanomaterials - current state, limitations, and needs*. Analytical and Bioanalytical Chemistry 417, 2405.
- Bleeker et al. (2023). *Towards harmonisation of testing of nanomaterials for EU regulatory requirements on chemical safety – A proposal for further actions* – Regulatory Toxicology and Pharmacology, 39, 105360.
- CCQM Task Group on Nano- and Microplastics Measurements and Standards, *CCQM Micro- and Nanoplastics Task Group National Metrology Laboratory Survey Results*.
- Minelli et al., (2022). *Versailles project on advanced materials and standards (VAMAS) interlaboratory study on measuring the number concentration of colloidal gold nanoparticles*. Nanoscale 14, 4690.
- Belsey et al., (2016) *Versailles project on advanced materials and standards interlaboratory study on measuring the thickness and chemistry of nanoparticle coatings using XPS and LEIS*. Journal of Physical Chemistry C 120, 24070.
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5.1.2 Particles in food and cosmetics.

General regulation and legislation:

- Cosmetics (Regulation (EC) 1223/2009)
- Food & Feed (Regulation (EC) No 178/2002)
- Information to consumers (Regulation (EU) 1169/2011)
- Contact materials (Regulation (EC) 450/2009)
- Novel foods (Regulation (EC) 2015/2283)
- Additives (Regulations (EC) 1331/2008, (EC) 1332/2008, (EC) 1333/2008, (EC) 1334/2008)
- Feed (Regulations (EC) 1831/2003, Regulation (EC) 429/2008)
- FDA Final Guidance for Industry: Safety of Nanomaterials in Cosmetic Products (FDA-2011-D-0489)
- FDA Final Guidance for Industry: Use of Nanomaterials in Food for Animals

EFSA guidance:

- Guidance on technical requirements for regulated food and feed product applications to establish the presence of small particles including nanoparticles (EFSA-Q-2019-00692, 2021).
- Physicochemical characterization of nanoparticles in food additives in the context of risk identification (EFSA-Q-2019-00502, 2021)

EC Scientific Committee on Consumer Safety guidance:

- Guidance on the safety assessment of nanomaterials in cosmetics (SCCS/1611/19, 2019).
- Hydroxyapatite (nano) - Submission IV (SCCS/1677/25, 2025)
- New coating for Titanium Dioxide (nano form) (SCCS/1667/24, 2024)
- Fullerenes, Hydroxylated Fullerenes and hydrated forms of Hydroxylated Fullerenes (nano) (SCCS/1649/23, 2023)

5.1.3 Nanomedicine and medical applications.

FDA Final Guidance for Industry:

- Drug Products, Including Biological Products, that Contain Nanomaterials (FDA-2017-D-0759)
- Considering Whether an FDA-Regulated Product Involves the Application of Nanotechnology (FDA-2010-D-0530)
- Liposome Drug Products: Chemistry, Manufacturing, and Controls; Human Pharmacokinetics and Bioavailability; and Labeling Documentation

EMA Scientific Guidelines:

- Data requirements for intravenous iron-based nano-colloidal products developed with reference to an innovator medicinal product – 2015
- Data requirements for intravenous liposomal products developed with reference to an innovator liposomal product – 2009
- Development of block-copolymer-micelle medicinal products – 2013
- Surface coatings: general issues for consideration regarding parenteral administration of coated nanomedicine products - 2013
- Nanotechnology-based medicinal products for human use - EU-IN Horizon Scanning Report (EMA/20989/2025/Rev. 1)

Other:

- Decision tree for navigating nanotechnology-based products for medical application (MHRA, 2025)
- Nelson et al. (2024). Toward an international standardisation roadmap for nanomedicine. Drug Delivery and Translational Research 14, 2578.

5.2 RELEVANT STAKEHOLDERS AND STAKEHOLDER GROUPS.

5.2.1 Particles in food and cosmetics.

Malta Initiative:

- Steer attention towards priorities for the work on test, measurement and verification procedures
- Support national and international exchange and cooperation
- Bring together different stakeholders in a constructive dialogue
- Strengthen trust in enforceable legislation and safe innovation
- Priority List for making OECD Test Guidelines and Guidance Documents applicable for Nanomaterials and Advanced Materials- March 2024

European projects:

NANOMET – Towards tailored safety methods for nanomaterials (2020-2023)
Gov4Nano - Meeting the needs of nanotechnology (2019-2023)
NanoHarmony - Towards harmonized test methods for nanomaterials (2020-2023)

5.2.2 Nanomedicine and medical applications.

Stakeholder platforms:

Nanomedicine European Technology Platform (ETPN)
NanoMeasureFrance - France

[Nanomedicines Innovation Network](#) – Canada
EUFEPS (EU Federation of Pharmaceutical Sciences) Network on Nanomedicine and Advanced drug delivery network.

European projects:

QuanTheriac - Metrology to support sustainable development of nanomedicines for therapy and theranostics (2026 – 2029)
METRINO - Metrology for Innovative NanoTherapeutics (2023-2026)
Phoenix - Pharmaceutical Open Innovation Test Bed for Enabling Nano-pharmaceutical Innovative Product (2020-2025)
EU-NCL - European Nanomedicine Characterisation Laboratory (2014-2019)
REFINE - Regulatory Science Framework for Nano(bio)material-based Medical Products and Devices (2017 – 2022)

5.3 RELEVANT METROLOGY ACTIVITY

5.3.1 Particles in food and cosmetics.

- Linsinger, et al. (2014). *International interlaboratory study for sizing and quantification of Ag nanoparticles in food simulants by single-particle ICPMS. Analytical and bioanalytical chemistry*, 406, 3835-3843.
- Geiss et al. (2021). *Particle size analysis of pristine food-grade titanium dioxide and E 171 in confectionery products: Interlaboratory testing of a single-particle inductively coupled plasma mass spectrometry screening method and confirmation with transmission electron microscopy*. Food Control,120, 107550.
- Weigel, et al. (2017). *Results of an interlaboratory method performance study for the size determination and quantification of silver nanoparticles in chicken meat by single-particle inductively coupled plasma mass spectrometry (sp-ICP-MS)*. Analytical and bioanalytical chemistry,409, 4839-4848.
- Henke, et al. (2024). *Interlaboratory comparison of centrifugal ultrafiltration with ICP-MS detection in a first-step towards methods to screen for nanomaterial release during certification of drinking water contact materials*. Science of The Total Environment, 912, 168686.

5.3.2 Engineered particles in air.

- Motzkus, et al. (2013). *Size characterization of airborne SiO2 nanoparticles with on-line and off-line measurement techniques: an interlaboratory comparison study*. Journal of Nanoparticle Research, 15, 1919.
- Carrasco, et al. (2023). *Inter- and Intra-Laboratory Comparison of 6 Dustiness Testing Methods: Towards the Development of an OECD Testing Guideline*. Annals of Work Exposures and Health, 67, i97.
- ISO 12025: Quantification of nano-object release from powders by generation of aerosols.
- ISO 15900: Determination of particle size distribution — Differential electrical mobility analysis for aerosol particles.
- ISO 18196: Measurement technique matrix for the characterization of nano-objects.
- ISO 19601: Aerosol generation for NOAA (nano-objects and their aggregates and agglomerates) air exposure studies.
- ISO 27891: Aerosol particle number concentration — Calibration of condensation particle counters.
- ISO 28439: Characterization of ultrafine aerosols/nanoaerosols –Determination of the size distribution and number concentration using differential electrical mobility analysing systems.

5.3.3 Nanomedicine and medical applications.

- Lehman et al., (2023). Particle Metrology Approach to Understanding How Storage Conditions Affect Long-Term Liposome Stability. Langmuir 39, 12313.
- Welsh, et al. (2020). Towards defining reference materials for measuring extracellular vesicle refractive index, epitope abundance, size and concentration. Journal of Extracellular Vesicles 9, 1816641.
- Jakubek et al. (2023). Lipid nanoparticle and liposome reference materials: Assessment of size homogeneity and long-term -70 ºC and 4 ºC storage stability. Langmuir 39, 2509.
- Syama et al. (2022). Development of lipid nanoparticles and liposomes reference materials (II) - Cytotoxic profiles. Scientific Report 12, 18071.

Documentary standards:

- ASTM E3482 - 25 Standard Guide for Characterization of Encapsulation, Extraction, and Analysis of RNA in Lipid Nanoparticle Formulations for Drug Delivery
- ASTM E3409-24 Standard Test Method for Analysis of Liposomal Drug Formulations Using Multidetector Asymmetrical-Flow Field-Flow Fractionation
- ASTM E3323-22 Standard Test Method for Lipid Quantitation in Liposomal Formulations Using High Performance Liquid Chromatography (HPLC) with an Evaporative Light-Scattering Detector (ELSD)
- ASTM E3324-22 Standard Test Method for Lipid Quantitation in Liposomal Formulations Using Ultra-High-Performance Liquid Chromatography (UHPLC) with Triple Quadrupole Mass Spectrometry (TQMS)
- ASTM E3297-21 Standard Test Method for Lipid Quantitation in Liposomal Formulations Using High Performance Liquid Chromatography (HPLC) with a Charged Aerosol Detector (CAD)
- ISO/TS 4958:2024 Nanotechnologies — Vocabulary — Liposomes
- ISO/TS 80004-7:2011 Nanotechnologies — Vocabulary Part 7: Diagnostics and therapeutics for healthcare

Pharmacopeial standards:

- EU Ph. 5.36. mRNA Vaccines for human use, covering the mRNA packaged in lipid nanoparticles, i.e. mRNA-LNP medicinal product
- EU Ph. 5.39. mRNA Substances for the production of mRNA vaccines for human use, i.e. the mRNA active substances in the manufacture of mRNA vaccines
- EU Ph 5.40. DNA Template for the preparation of mRNA transcript, i.e. the starting material for the preparation of the mRNA component.

Certified reference materials:

- ALNP-1: Anionic Lipid Nanoparticles by NRC Canada, with certified value for hydrodynamic diameter and polydispersity index.
- LNP-2: siRNA-loaded lipid nanoparticles by NRC Canada, with certified value for Z-average hydrodynamic diameter.
- ALIPO-1: Anionic Liposomes by NRC Canada, with certified value for hydrodynamic diameter and polydispersity index