European Partnership on Metrology
Call 2025 – Health, Integrated European Metrology, Regulation and Research Potential

Selected Research Topic number: **SRT-n09**
Version: 1.0

Title: Metrology for an internationally harmonised regulatory framework for nanomedicines

Abstract

Europe currently has over 22 % of the global nanomedicine market. Nanomedicine is the application of nanotechnology in healthcare i.e. using nanoscale materials and devices for disease prevention, diagnosis and treatment. Following the use of lipid nanoparticles in COVID-19 mRNA vaccines, the scope of nanomedicine products has been rapidly growing and diversifying, and now includes anticancer therapeutics, gene delivery platforms and personalised immunotherapies. However, in Europe, nanomedicines are not regulated by a specific regulatory framework, but instead fall under existing frameworks for medicinal products and devices. The European Medicines Agency (EMA) currently provides guidelines for nanomedicine developers, but these are not mandatory. Thus, there is an urgent need for a specific regulatory framework for nanomedicines, supported by accurate metrological methods, associated reference materials and reference datasets. Also needed is regulation for nanomedicine manufacturing and advances in the analytical and digital technologies used to ensure nanomedicine product quality assurance, control and safety.

Keywords

Nanomedicines, lipid nanoparticles, complex therapeutics, sustainable manufacturing, analytical technology, digital technology, quality assurance, disease prevention

Background to the Metrological Challenges

The global nano-pharmaceuticals market was worth approx. $36 billion in 2024 and is predicted to rise to $91 billion by 2032. Within this market, lipid nanoparticles/liposomes account for the largest share, having been brought to public attention by the COVID pandemic and their use in COVID-19 mRNA vaccines. Over the last 50 years, the use of nanomedicines has been rapidly diversifying. New nanomedicine products now include chemotherapy drugs that use nanotechnology to enhance their delivery and efficacy in cancer treatment, dual-drug systems (e.g. which deliver two different drugs in liposomes), localised administration and biological delivery (e.g. mRNA vaccines, which use lipid nanoparticles to encapsulate and deliver mRNA to target cells, protecting the mRNA from degradation and facilitating its entry into cells). However, despite their usage and potential benefits to health, there is currently no specific European framework for nanomedicines. Instead, existing frameworks for medicinal products (Directive 2001/83/EC and Regulation (EC) No 726/2004) and medical devices (Directive 93/42/EEC) must be used.

Another advantage of nanomedicines is their green credentials. There is increasing pressure for pharmaceutical industries to adopt greener processes, with more efficient use of resources, reduced waste and using greener chemistries. Lipid-based nanomedicines are largely produced by microfluidics, or in small batches for personalised applications, thus they are well suited to manufacturing approaches that reduce factory waste (e.g. continuous manufacturing) and the need for transportation (e.g. distributed manufacturing). But there are currently no specific regulatory requirements for nanomedicine products manufactured through these approaches.

The 2024 Reform of the EU pharmaceutical legislation recommends "*Additional…..regulatory support by EMA for medicines which address unmet needs or represent a major therapeutic innovation*". This is true for nanomedicines which exhibit significant complexity compared to traditional small molecule therapeutics. However, because of the variety and complexity of nanomedicines, measurement standards for their quality, safety and efficacy can only be developed on a case-by-case basis, which is time consuming and costly.

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Currently, the measurement technologies available for use with nanomedicines are only partially standardised and lack validation for structurally and chemically complex nanomedicines. For example, CIPM Consultative Committee for Amount of Substance: Metrology in Chemistry and Biology (CCQM) and VAMAS Technical Working Area 34 (TWA34 Nanoparticle Populations) have undertaken interlaboratory comparisons but only on number concentration for ideal solid, spherical nanoparticles (i.e. CCQM P210 and VAMAS TWA34 P10). In terms of reference materials, NRC (the NMI for Canada) has recently developed liposome and lipid nanoparticle certified reference materials, but these are currently only certified for size. Recently, NIST (the US NMI) has also initiated the development of mRNA-loaded lipid nanoparticle reference materials, but work is still on-going.

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 regulation for the use of nanomedicines.

The specific objectives are

1. To identify, map and prioritise current and future metrology needs for nanomedicines using input from key stakeholders, in particular European regulators and standardisation experts from the EMA, CIPM-CCQM, CEN/TC 352 (Nanotechnologies), ISO/TC 229 (Nanotechnology), ISO/TC 276 (Biotechnology), the European Directorate for the Quality of Medicines and Health Care (EDQM), the International Pharmaceutical Regulator Programme (IPRP), the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) and the American Society for Testing and Materials (ASTM) E56.8 (Nano-enabled medical products). The metrology needs must include nanomedicine manufacturing and qualification, for both generics and (bio)similar products. The outcomes should be produced in formats suitable for disseminating to regulatory and standards bodies, NMIs/DIs, the pharmaceutical industry and broader stakeholders.
2. Using input from Objective 1, to map and prioritise regulatory, metrology, technology solution and data quality requirements for the adoption of greener processes for manufacturing and distributing nanomedicines. This will include (i) continuous manufacturing, (ii) distributed manufacturing, (iii) digitally-assisted manufacturing, and (iv) low batch volume manufacturing. Then using the results, produce at least 2 case studies, demonstrating and quantifying efficiencies in nanomedicine manufacturing using improved analytical and digital methods (e.g. in/on/at line analysis, digital twins). The case studies should demonstrate how innovative metrology can support these endeavours
3. Based on the needs in Objectives 1 and 2, to develop reference materials for lipid-based nanoparticles and associated measurement methods for their characterisation. Then to test, validate and benchmark these reference materials and methods through at least 3 interlaboratory comparisons. The results will be used to produce (i) good practice guidelines for measuring nanomedicines, (ii) reference datasets, and (iii) at least 4 pharmacopeial monographs for nanomedicines.
4. To contribute to the standards development work of the technical committees CEN/TC 352, ISO/TC 229, ISO/TC 276, EMA, EDQM, IPRP and ICH, related to the regulation of nanomedicines 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 provided in a form that can be incorporated into the standards at the earliest opportunity.

The proposed research shall respond to documented requirements related to specific regulations and legislation or explore the background and feasibility of expected possible future regulation. To enhance the impact of the research, the involvement of the appropriate user community such as regulatory authorities, conformity assessment bodies, standardisation bodies, and industry, is strongly recommended. Where relevant, proposals are encouraged to build on, or seek collaboration with, existing projects and develop synergies with other relevant European, national or regional initiatives and funding programmes. In particular, links are encouraged with (i) the projects funded under earlier relevant topics of the Horizon Europe programme; or (ii) other relevant European Partnerships.

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 Metrology Partnership projects 22HLT04 MetrINo and 23NRM02 SMURFnano 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 healthcare, nanomaterial and pharmaceutical sectors and regulatory authorities.

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.

These references have been provided by EURAMET.

[1]. *003 CEN TC 352 B2B traceability and B2C regulatory compliance nanomaterial products* https://metpart.eu/applicants-2025/regulation-call-2025-s1.html

[2]. *Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use* http://data.europa.eu/eli/dir/2001/83/oj

[3]. *Council Directive 93/42/EEC of 14 June 1993 concerning medical devices* http://data.europa.eu/eli/dir/1993/42/2007-10-11

[4]. EMN Traceability in Laboratory Medicine (TraceLabMed) Strategic Research Agenda https://www.euramet.org/research-innovation/metrology-partnership/strategic-research-and-innovation-agendas

[5]. EMN for Advanced Manufacturing Strategic Research Agenda https://www.euramet.org/research-innovation/metrology-partnership/strategic-research-and-innovation-agendas