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

Selected Research Topic number: **SRT-h15**
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Title: Metrology to ensure rapid and accurate diagnostic response to current and emerging infectious diseases

Abstract

Infectious diseases cause pandemic (COVID), epidemic (Zika) or endemic (influenza) infections. These outbreaks cause major societal challenges to healthcare and the economy. Rapid and accurate diagnostics is often the only healthcare tool that can be used to manage current and emerging infectious diseases and to prevent further spread. However, these diagnostic tools are often poorly standardised and analytical accuracy has not been central to their development or wider deployment. Therefore, a metrology infrastructure needs to be developed to improve standardisation, quality assurance and the traceability of measurements with the aim of significantly improving the detection of, and response to, acute and emerging infectious diseases.

Keywords

Diagnostic accuracy, epidemic prevention, epidemiology, infection, in vitro diagnostic test, laboratory tests, pathogen, point of care

Background to the Metrological Challenges

Accurate and approved rapid in vitro diagnostic (IVD) tests for infectious diseases are needed for pathogen detection, for the development and application of treatment, for contact tracing, and public health decision-making, at national and global levels. These tests, which often use bioanalytical technologies that detect DNA, RNA or protein molecules were crucial in the response to the COVID-19 pandemic and continue to represent the first line of defence for the identification of pathogens and the initiation of a therapeutics and vaccine response.

Despite this, stakeholders are often unaware of the value of metrology in enabling the accurate and confident use of IVDs, and the systems needed to ensure traceability, quality assurance, or continuity of unit, remain in their infancy. The limited reference measurement infrastructure frequently forces IVD manufacturers to develop solutions in isolation, unsupported by routes to assure accuracy. This likely hindered the responses to COVID-19, Zika and Mpox as epidemiological decisions were made from IVD results of unknown accuracy. Consequently, metrological principles need to be built into IVD guidelines and regulations to prevent this.

World Health Organization (WHO) reference materials exist to support test calibration, use international units without measurement uncertainty, and are relatively slow to establish. They have revolutionised harmonisation, but they focus on diseases where quantification is needed for clinical management. Conversely semiquantitative or nominal (presence/absence) IVDs are viewed as simpler to standardise, which, depending on analyte quantities, may be a mistake. Reference measurement procedures are not used to determine reference ranges nor to value assign reference materials. Consequently, IVDs with different analytical performance are selected without the quantitative foresight to predict how they will work. The evaluation of point of care tests (lateral flow devices (LFDs) or biosensors) is typically limited to patient samples of unknown, or poorly quantified, analyte ranges with poorly documented provenance and pre-analytics. Therefore, it is unclear how the billions of LFDs used in Europe during the COVID-19 pandemic differed in performance. The public acceptance of at home testing is a huge public health opportunity, but metrology is urgently required across these bioanalytical test modalities to realise its potential. These metrological limitations need to be addressed, with consideration of clinical factors, through improved performance evaluation and a wider reference measurement and standardisation infrastructure, both in the laboratory, and at the point of care. This

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has been highlighted as a priority in the European Metrology Network for Traceable Laboratory Medicine orientation paper for the Metrology Partnership Health call 2025 [1].

In addition to the shortcomings in IVD metrology, assumptions about disease dynamics have led to the oversimplification of diagnostic performance evaluation and considerable error. For example, the pathogen detection and conformity assessment criteria, specified in EU documentation, currently focus on conventional sensitivity / specificity testing and classification methods. In reappraising these techniques, using artificial intelligence (AI) and machine learning (ML), recent advances in the metrology of nominal properties suggest that a generic methodology, for classification device characterisation, should be piloted for infectious disease diagnosis. Therefore, alternatives to longitudinal changes in classification rates of success, or threshold setting, and potential wider areas of application, including remote diagnosis, need to be investigated. This will require state-of-the-art metrological methods to be expanded for better evaluation of diagnostic pipelines including the development of statistical and measurement-system approaches, which will be superior to traditional performance metrics. AI and ML approaches also need to be refined to advance this process.

IVD manufacturers, users and those tasked with their regulation face considerable challenges when developing and deploying tests for pathogens. Advisory, or legally binding, targets are challenging to define for the complex measurands targeted by bioanalytical IVDs especially when considering new pathogens. Therefore, work needs to be undertaken in close collaboration with stakeholders from industry, healthcare, academia and the regulatory networks (EU reference laboratories (EURLs), notified bodies, etc.) to deliver solutions that support test development, wider roll out and post market evaluation for routine infection testing and in preparing for pandemics or infectious disease outbreaks.

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 the development of metrology to ensure rapid and accurate diagnostic responses to current and emerging infectious diseases.

The specific objectives are

1. To establish a reference measurement infrastructure to ensure accurate pathogen diagnosis. This should include (i) the implementation of SI traceable reference measurement procedures and materials, with a < 20 % expanded uncertainty, to support safe and vertical quality assurance and (ii) the development of systems to support accurate diagnosis, through a swift metrological response, which can be adapted to epidemiological changes.
2. To optimise measurement strategies, by reviewing clinical data sets, and to provide alternative routes for diagnostic evaluation. This should include (i) the development of models to characterise analytes and reference ranges in order to guide the evaluation of tests, threshold setting and to evaluate the impact of clinical sensitivity shifts on diagnostic performance, and (ii) the use of state-of-the-art metrological methods to better evaluate the in vitro diagnostics (IVD) performance of measurement devices including the use of item response theory for classification characterisation by using artificial intelligence (AI), machine learning (ML) and internet of things (IoT).
3. To apply measurement infrastructure to IVD development, application and post market monitoring. This should include (i) collaboration with IVD manufacturers, clinical labs and EU reference laboratories (EURLs) to implement methods to improve centralised, and point of care, test evaluation, including the provision of dynamic responses to epidemiological change, (ii) the provision of standards, and (iii) an evaluation of innovative diagnostic methods such as biosensors and novel detection / identification methods (e.g. based on clustered regularly interspaced short palindromic repeats).
4. To implement metrology for analytical targets in guides and regulatory documents. This should include: (i) community materials certified for identity, provenance, genetic variability, etc., (ii) target specimen profiles tailored to support the development and validation of novel tests, (iii) generalised standards where bioanalytical concepts are less clear (e.g. measurand definition). In addition, an IVD traceability group should be established, which should focus on identifying and meeting the challenges, and clinical needs, associated with seasonal and outbreak pathogens.

5. To facilitate the take up of the technology and measurement infrastructure developed in the project by the measurement supply chain (EURAMET TC-MC, CIPM CCQM, Joint Committee for Traceability in Laboratory Medicine), standards developing organisations (ISO TC212, ISO TC276, CEN TC 140), end users (e.g. clinical stakeholders, manufacturers of medical and healthcare products, international organisations focussed on clinical diagnosis (ESCMID, IFCC, WHO, EURLs, MDCG), IVD providers).

These objectives will require large-scale approaches that are beyond the capabilities of single National Metrology Institutes and Designated Institutes, and it is expected that multidisciplinary teams will be required. To enhance the impact of the research, the involvement of the appropriate user community such as medical practitioners, medical (academic) hospitals and industry is strongly recommended, both prior to and during methodology development. 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 project goes beyond this. In particular, proposers should outline the achievements of the EMPIR projects NEW04 CASoft, 15HLT04 NeuroMET, and 18HLT09 NeuroMET2 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 2.1 M€ and has defined an upper limit of 2.6 M€ for this proposal.

EURAMET also expects the EU Contribution to the external funded beneficiaries to not exceed 35 % 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 medical and health 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 link provided in this section is only correct at the time of publication up until the end of the Call year.

This reference has been provided by EURAMET.

[1] Orientation Paper by EMN for Traceable Laboratory Medicine, https://metpart.eu/applicants-2025/health-call-2025-s1.html