

Publishable Summary for 25HLT01 XMET

Metrology to ensure rapid and accurate diagnostic response to current and emerging infectious diseases

Overview

XMET will strengthen the accuracy, comparability and clinical value of infectious-disease diagnostics by providing the metrology needed to underpin confidence in testing. Current bioanalytical in-vitro diagnostic (IVD) tests, including polymerase chain reaction (PCR) and lateral flow devices, lack robust reference systems to ensure traceability and reproducibility. This project will build a comprehensive measurement infrastructure combining reference methods, well characterised materials, advanced statistics and clinical evaluation strategies. XMET will work closely with IVD manufacturers, regulators, laboratories and public health agencies to develop the metrology to support testing for routine infectious diseases and emerging pandemics threats.

Need

Infectious diseases remain a leading cause of global morbidity and mortality across Europe and the wider world. Diagnostic tests that detect pathogen associated biomolecules are widely used in health care and often represent the first step in confirming aetiological cause. These IVDs are frequently described as critical to disease management, while also providing epidemiological information to guide public health decisions. Yet these tests are often difficult to standardise due to inherent complexities associated with the analytes and the fact the samples, like a nasal swab, may be highly variable and challenging to obtain. During COVID-19, widely used PCR tests showed 10,000-fold differences in reported limits of detection, while antigen and point of care tests were deployed in the absence of reference measurement systems to underpin analytical accuracy or post market surveillance.

Essential regulatory frameworks, including the In Vitro Diagnostic Regulation (EU) 2017/746 (IVDR), require metrological traceability to enable manufacturers to demonstrate performance, yet such traceability currently does not exist for most bioanalytical infectious disease IVDs. This diagnostic deficit affects everything from patient management and antimicrobial stewardship to epidemiological modelling and public health decision making. Without reference measurement systems, IVD developers cannot reliably calibrate assays, external quality assurance (EQA) schemes cannot assign true values, regulators lack objective means to judge performance, and healthcare systems remain vulnerable to inaccurate testing during outbreaks. XMET addresses this urgent gap by establishing the metrological foundations necessary for trustworthy, rapid diagnostics applicable to pathogens such as influenza, tuberculosis, mpox and future disease X agents.

XMET addresses this urgent gap by establishing the metrological framework in objective 1 and, guided by clinical factors determined by objective 2, apply this to support EQA, regulatory assessment, post market surveillance and research and development of infectious disease IVDs. This will provide the foundation necessary for trustworthy, diagnostics applicable to known pathogens such as influenza, drug resistant tuberculosis, and mpox, as well as preparing for future disease X agents.

Objectives

XMET will provide a mechanism to deliver metrological traceability for bioanalytical IVDs to improve test accuracy and confidence and facilitate their alignment to regulatory standards including the in vitro diagnostic regulation (IVDR).

Report Status:
PU – Public, fully open

Publishable Summary

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European Partnership

Co-funded by the European Union

METROLOGY PARTNERSHIP



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The specific objectives of the project are:

1. To establish a reference measurement infrastructure to enable accurate pathogen diagnosis for infectious diseases based on (i) the development of SI traceable reference measurement procedures (e.g. digital PCR and Isotope Dilution Mass Spectrometry - IDMS) and materials (ranging from synthetic bio analytes in buffered solutions to whole pathogens in more complex biological matrices) with a <20 % expanded uncertainty suitable for inclusion in the joint committee for traceability in laboratory medicine (JCTLM) database and (ii) the development of reference measurement systems to support accurate diagnosis of infectious diseases based on prototype calibration hierarchies for nucleic acids and antigens with suitability for bioanalytical testing to support metrological traceability as outlined by the IVDR.
2. To optimise measurement strategies and to improve the application of clinical concepts into diagnostic evaluation by (i) reviewing clinical data sets to determine concentrations, the identity and ranges of pathogen analytes within clinical specimens used as IVD device (IVDD) and samples performance, (ii) investigating the use of state-of-the-art metrological methods to better evaluate the performance of the IVDD measurement and samples including the use of item response theory (IRT) for classification characterisation and then based on these results (iii) conducting a clinical performance evaluation of IVD devices and samples in both centralised and decentralised bioanalytical in vitro diagnostic tests for infectious diseases.
3. To apply the developed measurement infrastructure for infectious diseases from Objectives 1 and 2 to support IVD development, application and post market monitoring. This will include (i) a metrological assessment of bioanalytical IVDs by EU reference laboratories (EURLs) with the provision of dynamic responses to epidemiological change to implement methods to improve centralised, and point of care tests (POCT) evaluations, (ii) developing routes to ensure a timely metrological response in pandemic scenarios, and the provision of physical standards for EQA (including for pandemic response super challenge), and (iii) a metrological evaluation of innovative diagnostic methods such as biosensors and novel detection / identification methods.
4. To implement metrology for analytical targets in guides and regulatory documents and facilitate the take up of the technology and measurement infrastructure developed in the project by the measurement supply chain (EURAMET TC-MC, CIPM CCQM, JCTLM), 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).

Progress beyond the state of the art and results

Objective 1: To establish a reference measurement infrastructure to enable accurate pathogen diagnosis for infectious diseases

EMPIR projects have developed reference methods, materials and protocols for bioanalysis, but no project has established a complete calibration hierarchy applicable across infectious disease diagnostics.

XMET will integrate SI-traceability, reference methods, WHO materials and uncertainty evaluation to provide robust dynamic measurement systems to support comparable results across technologies and laboratories.

Objective 2: To optimise measurement strategies and to improve the application of clinical concepts into diagnostic evaluation

Clinical evaluation of infectious disease IVDs is often based on heterogeneous clinical specimens and comparison with existing diagnostic methods, with limited integration of metrological approaches and clinical characteristics of the samples.

XMET will use clinical datasets to define the concentration, identities and ranges of pathogens in clinical specimens. This will inform optimised measurement strategies and the application of advanced metrological and statistical approaches. These approaches will support the evaluation of the clinical performance of IVDs and samples in centralised and decentralised infectious disease testing. This will strengthen the link between clinical characteristics, measurement performance and diagnostic classification.

Objective 3: To apply the developed measurement infrastructure for infectious diseases from Objectives 1 and 2 to support IVD development, application and post market monitoring

Metrological support for IVD development, evaluation and post-market surveillance is not yet sufficiently integrated or responsive to emerging epidemiological threats, with limited access to physical standards for EQA and pandemic preparedness. Evaluation frameworks for innovative technologies such as biosensors, novel detection and identification methods also remain underdeveloped.

XMET will apply the measurement infrastructure developed in Objectives 1 and 2 through a EURL metrological assessment of bioanalytical IVDs. This will support the improved evaluation of both centralised tests and POCTs and enable dynamic responses to epidemiological change. It will establish routes for timely metrological responses during pandemics, including physical standards for EQA “super challenges”, while also extending metrological evaluation to innovative diagnostic technologies such as biosensors, novel detection and identification methods.

Outcomes and impact

Key dissemination and communication activities

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Outcomes for industrial and other user communities

XMET will deliver advanced measurement tools and reference systems to help IVD manufacturers, clinical laboratories, and public-health institutions to improve the accuracy of tests for both routine and emerging infectious diseases. XMET will establish a metrological infrastructure designed for integration into real-world testing. Clinical laboratories, EURLs, government health organisations and IVD manufacturers will be involved from the start, ensuring methods and materials are operationally relevant and rapidly disseminated through networks such as EURAMET’s European Metrology Network for Traceability in Laboratory Medicine (EMN-TLM).

Early benefits will come from collaboration with EQA providers. XMET will support assignment of accurate reference values and comparison of reference methods with clinical assays. Currently, many EQA providers lack the reference methods required to assign reference values to materials for the specific analytes being evaluated. XMET will expand this capacity and establish rapid routes for reference procedure development to support testing deployed in outbreak prevention, including low- and middle-income countries (LMIC), enhancing global diagnostic capacity.

For IVD manufacturers, XMET will provide the tools to calibrate, characterise, and evaluate technologies, supporting compliance with the IVDR, including for neglected diseases where standard materials are lacking. SI-traceable reference systems will enable traceable calibration of rapid tests, improve reliability, and strengthen preparedness for future pandemics. Regulators, public-health agencies, and clinical laboratories will be included early in the project and benefit from tools to select and monitor the performance of tests at the local, national and international level.

Outcomes for the metrology and scientific communities

XMET will build on existing links (<https://www.euramet.org/european-metrology-networks/laboratory-medicine>) and create a multidisciplinary network linking NMIs, reference-material and EQA providers with clinical experts and the diagnostic research and development community. XMET will expand bioanalytical capabilities for nucleic acids, proteins, and other biomolecules, supporting reproducible measurement across assay types. Participants’ involvement in CCQM comparisons will strengthen calibration and measurement capabilities and extend benefits to research laboratories and diagnostics, including in LMICs. Well-characterised materials will improve evaluation of analytical performance, limits of detection, and matrix effects.

For the scientific research community, XMET will provide reproducible measurement frameworks that enhance reliability of pathogen biology, epidemiology, and diagnostic studies. Standardisation will improve cross-laboratory comparisons, multi-site studies and clinical trials. Training and capacity-building will increase expertise in bioanalytical measurement, while links with WHO, ECDC, ESCMID, and IFCC will ensure global dissemination. XMET outputs will support reproducible science, informed public-health decisions, and global preparedness.

Outcomes for relevant standards

XMET will strengthen international standards by developing dynamic reference measurement systems, higher-order reference methods, and quality-assurance tools. Many bioanalytical techniques used in infectious-disease testing currently lack robust traceability. XMET will enable standardised calibration, harmonised reporting, and consistent interpretation of results.

The project will directly support compliance with EU IVDR and address gaps in standards for neglected diseases. Participants hold leadership or expert roles in ISO TC212, ISO TC276, CEN, CLSI, JCTLM, EURAMET, CCQM, WHO, and other bodies. These roles ensure that the outputs of these organisations inform revisions of standards for diagnostics, pandemic-response tests, and laboratory quality management. Harmonised reference materials and procedures will embed traceability in global standards, enabling comparable diagnostic results worldwide.

By aligning with international standardisation efforts, XMET provides the regulatory and scientific communities with foundations to modernise diagnostic standards, strengthen pandemic preparedness, and support reliable laboratory medicine, reinforced by links with EMN-TLM, IFCC, ESCMID, WHO, ECDC, The African CDC and Pan American Pathogen Networks.

Longer-term economic, social and environmental impacts

XMET's focus on improving pathogen IVD accuracy has the potential to deliver significant economic and societal benefits. Infectious diseases impose enormous costs; seasonal influenza alone is estimated to cost (just) the UK over £600 million in lost productivity each year. Accurate diagnostics enable timely interventions, outbreak containment, and effective pandemic response. By reducing this metrological deficit, XMET will improve the test information available to be used to make healthcare decisions at both the individual and population level. The growing IVD market, projected to exceed \$30 billion by 2028, will directly benefit from a strong metrological foundation, reducing uncertainty, de-risking innovation, accelerating development, and strengthening Europe's competitiveness.

The project also aligns very closely with international pandemic-preparedness efforts, including the 100 Days Mission overseen by the International Pandemic Preparedness Secretariat (IPPS). In its 2025 diagnostic gap analysis, the Secretariat emphasised the need for developers to work with metrology institutes to embed reference measurement systems early in product design. This approach, which is pivotal to XMET, will improve analytical validation of IVD testing, which is often also central in supporting the assessment of novel therapeutics and vaccines, and it will strengthen response and recovery efforts during future pandemics.

XMET is dedicated to improving the integration of the metrology community with those who are tasked with developing, applying and regulating bioanalytical IVDs to support pathogen test accuracy in routine infectious disease diagnostics and outbreak response to deliver meaningful economic and societal benefits.

List of publications

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This list is also available here: <https://www.euramet.org/repository/research-publications-repository-link/>

Project start date and duration:		1 August 2026, 36 months
Coordinator: Jim Huggett, LGC		
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Project website address: https://www.uknml.com/about-us/our-international-role/european-projects/xmet/		
Internal Beneficiaries:	External Beneficiaries:	Unfunded Beneficiaries:
1. LGC, UK	8. BGU, Israel	21. INM CO, Colombia
2. LNE, France	9. BH, UK	
3. MHRA, UK	10. CEA, France	
4. NIB, Slovenia	11. GBD, Germany	
5. NPL, UK	12. IH, UK	
6. RISE, Sweden	13. INSTAND, Germany	
7. TUBITAK, Türkiye	14. KRISS, Republic of Korea	
	15. LSTM, UK	
	16. MIB, Germany	
	17. ÖQUASTA, Austria	
	18. Pasteur, France	
	19. PEI, Germany	
	20. UMK, Poland	