

Draft template for biennial activity report from JCTLM Member organizations

All JCTLM Members are invited to attend the Members' and Stakeholders' Meeting, which is held once every two years, and submit a report of their activities in support of traceability in laboratory medicine over the preceding period.

For that purpose this template document provides guidance to JCTLM Members for drafting their biennial activity report. Organizations are invited to provide the information below for submission to the Executive Committee.

Organization Name: National Measurement Laboratory (LGC) (UK)

JCTLM Member status: National and Regional Member

Author(s): Alison Devonshire, Luise Luckau, Jeanne Rivera, Laura Carrick-White, Maya Petrova, Caroline Pritchard, Denise O'Sullivan, Carole Foy, Tabatha Hambidge, Emily Whyte, Christian Ward-Deitrich, Kharmen Billimoria, Jim Huggett, Heidi Goenaga-Infante, Julian Braybrook.

Author(s) email(s): alison.devonshire@lgcgroup.com

Period covered: 2024 – 2025

1. Major achievement(s) in support of standardization in laboratory medicine

(Please describe what activities your organization has undertaken related to the implementation of reference measurement systems in laboratory medicine during the last two years, including but not limited to information on: the production of certified reference materials; the development of reference measurement methods; or the establishment of calibration (reference) measurement services. Outline the measurement area(s)/measurands covered, and provide a listing of the relevant technical/scientific publications.)

Protein measurements:

- Development of a candidate reference measurement procedure for alpha-synuclein quantification in cerebrospinal fluid (CSF) under 15HLT09-NeuroMET and 18HLT09-NeuroMET2 (Publication: "A candidate reference measurement procedure for the quantification of α -synuclein in cerebrospinal fluid using an SI traceable primary calibrator and multiple reaction monitoring" Leran Zhang et al, *Analyst*, 2024,149, 4842-4850)
- Structural characterization of neurofilament light chain primary calibrator used for the development of a candidate RMP under 15HLT09-NeuroMET and 18HLT09-NeuroMET2 (Publication: "Neurofilament Light Chain under the Lens of Structural Mass Spectrometry" Salome Coppens et al, *ACS Chem Neurosci*. 2025 Jan 15;16(2):141-151. doi: 10.1021/acchemneuro.4c00526.)
- Development of a quantification method for neurofilament light chain in CSF using immunoprecipitation, funded from the European Union's Horizon 2020 research and innovation program Marie Curie ITN 'MIRIADE' under the grant agreement number 860303 and 22HLT07 NEuroBioStand. (Publication: "Development of a novel LC-MRM assay for the quantification of neurofilament light chain in cerebrospinal fluid and comparison with ultra-sensitive immunoassay: a step toward standardization" Salome Coppens et al, *Clinical Chemistry*, accepted on 17.11.2025)
- SI value assignment of a WHO standard for Ferritin Light Chain using species-specific HPLC-ID-ICPMS *via* sulfur. Publication: "Species-Specific Isotope Dilution Methodology for the SI Traceable Quantification of Serum Human Ferritin Light Chain (FTL)" Christian Ward-Deitrich et al, *Anal Chem*. 2025 Nov 13. doi: 10.1021/acs.analchem.5c04597
- Selenoproteins like Selenoprotein P in human serum by species-specific HPLC-ID-ICPMS *via* selenium. Accurate Quantification of Selenoprotein P (SEPP1) in Plasma Using Isotopically Enriched Seleno-peptides and Species-Specific Isotope Dilution with HPLC Coupled to ICP-MS/MS. Christian L. Deitrich et al., 2016. *Anal. Chem.* 88 (12), 6357–6365. <https://doi.org/10.1021/acs.analchem.6b00715>; Selenium speciation studies in cancer patients to evaluate the responses of biomarkers of selenium status to different selenium

compounds, M. E. Del Castillo Busto, et al., Anal. Bioanal. Chem., 2024, <https://doi.org/10.1007/s00216-024-05141-y>

Metabolite measurements

- Development of a value assigned Phenylalanine plasma material to underpin an international EQA scheme “Development of an SI traceable value assigned amino acid matrix-matched material to underpin European external quality assessment” Whyte et al. Published in Analytical and Bioanalytical Chemistry Vol. 417 February 24, 2025. DOI: [10.1007/s00216-025-05793-4](https://doi.org/10.1007/s00216-025-05793-4)

Nucleic acid measurements

Standardisation of SARS-CoV-2 RNA measurements – publication of candidate RMP and organisation of CCQM key comparison study which was coordinated by NIM, LGC and MHRA:

- Samreen Falak, Denise M O’Sullivan, Megan H Cleveland, Simon Cowen, Eloise J Busby, Alison S Devonshire, Esmeralda Valiente, Gerwyn M Jones, Martin Kammel, Mojca Milavec, Laura Vierbaum, Ingo Schellenberg, Heinz Zeichhardt, Andreas Kummrow, Peter M Vallone, Rainer Macdonald, Jim F Huggett, The Application of Digital PCR as a Reference Measurement Procedure to Support the Accuracy of Quality Assurance for Infectious Disease Molecular Diagnostic Testing, Clinical Chemistry, Volume 71, Issue 3, March 2025, Pages 378–386, <https://doi.org/10.1093/clinchem/hvae187>
- Lianhua Dong, Xinhua Dai, Chunyan Niu, Xia Wang, Jie Xie, Xiang Fang, Alison Devonshire, Jim Huggett, Clare Morris, Neil Almond et al 2025 CCQM-K181 SARS-CoV-2 RNA copy number quantification. Metrologia **62** 08016. DOI 10.1088/0026-1394/62/1A/08016.

Standardisation of HER2 copy number variation measurements (breast cancer biomarker): organisation of CCQM-K176 with NIM, and achievement of a Calibration and Measurement Capability (CMC) together with ISO 17025 (2017) fixed scope accreditation for HER2 testing:

- Lianhua Dong, Xia Wang, Alison Devonshire, Jim Huggett, et al 2024 CCQM-K176 breast cancer biomarker HER2 copy number variation (CNV) measurement. Metrologia **61** 08017. DOI 10.1088/0026-1394/61/1A/08017.

2. Planned activity(ies) in support of standardization in laboratory medicine

(Please outline R&D project(s) and/or programme(s) planned by your organization in the next two years including information on: new measurement area(s)/meurands of interest for your organization; new CRMs and renewals of materials; development of methods (new measurands and improved measurement technique/principle); and extensions of your calibration measurement service(s) portfolio.)

New RM/CRMs:

- Development of CRMs for pure Cyclosporin A and Cyclosporin A in a biological matrix
- Development of CRMs for tacrolimus and sirolimus in whole blood
- Development of a prototype CRM for neurofilament light chain in CSF and serum
- Development of a candidate RM/QC material for digital PCR platform validation and comparison
- Potential development of a 17 β -estradiol pure material

CCQM study participation/coordination and extensions of testing / calibration services:

- Coordination / participation in upcoming CCQM study CCQM-K115.e (cyclosporin A quantification)
- Coordination / participation in CCQM-K189 (Quantification of cancer genetic variants in genomic DNA)
- Coordination / participation in CCQM-K190 (Quantification of SARS-CoV-2 RNA in whole virus)
- Coordination / participation in CCQM-K198 (Quantification of cancer genetic variants in cell-free DNA)
- Extension of measurement capabilities to small proteins without modification (participated in CCQM-K115d 1-84 quantification, ongoing CCQM-P257)
- Extension of measurement capabilities to include peptides/proteins with modifications (CCQM-K115e cyclosporin A)
- Coordination / participation in upcoming CCQM pilot study on laser ablation ICPMS, supporting bio-imaging measurements relevant to cancer biomarker research and digital pathology.
- Participation in CCQM-K192 (17 β -estradiol in human serum)

- Coordination / participation in 2027 CCQM track A key comparison (Sirolimus in whole blood)

Measurement research programme:

- Development of a RMP for natriuretic peptide (NT-proBNP) quantification in serum/plasma
- Development of a RMP for neurofilament light chain quantification in serum/plasma
- Development of RMPs for solid tumour / liquid biopsy somatic variants (DNA)
- Development of RMPs for leukaemia molecular minimal residual disease (MRD) biomarkers (RNA)
- Development of RMPs for influenza RNA measurements
- Development of RMP for critical quality attribute assessment using morphological cell profiling for identification of Type 2 diabetic endothelial cells by brightfield flow cytometry
- Development of methods to determine key morphological parameters to support biomarker expression and cell identification for red blood cells using brightfield flow cytometry
- Development of methods to evaluate image analysis tools for improved cell characterisation and quantification of fluorescence and brightfield data
- Development of methods to characterise extracellular vesicles as biomarker for gestational diabetes
- Development of RMP for ceramides in biological matrices as biomarkers for cardiovascular diseases
- Development of automated methods for traceable value assignment of small molecules to enable rapid assignment of materials to support the metabolomics community
- Development of traceable mass spectrometry-based methods to support RNA and DNA measurements

Measurands of Interest:

Protein measurements:

- Albumin, IGF-1
- SI-traceable quantification of antibodies
- Host-cell protein quantification relevant for protein material (e.g. recombinant antibodies, viral vector) characterization
- Quantification of structurally related protein impurities
- Infectious disease antigen testing

Nucleic acid measurements:

- Solid tumour / liquid biopsy genetic and epigenetic biomarkers
- Monkeypox virus DNA
- *Mycobacterium tuberculosis*
- Antimicrobial resistance markers

Cell measurements:

- Red blood cells (derived from Paroxysmal nocturnal hemoglobinuria)
- Endothelial cells derived from skeletal and adipose tissue
- PBMCs
- Mass of delivered drug at the single cell level per number of cells
- Cell imaging

Small organic molecule measurements:

- Immunosuppressants
- Lipids (ceramides, LNP composition)
- Metabolomics targets (amino acids, acylcarnitines, lipids, steroid hormones)
- Oligonucleotides
- Selenium species e.g. SeMet
- Organo-chromium species

Particle measurements:

- LNPs with encapsulated drugs
- LNP-mRNAs
- Exosomes
- Gene therapy delivery vectors / Virus-like Particles

3. Promoting traceability in laboratory medicine

(Please describe activities your organization has undertaken during the last two years for promoting traceability in laboratory medicine including but not limited to a listing of your publication(s), presentation(s) and other communication(s) on traceability at international and national conferences or congresses, or other forums for clinical laboratory medicine)

Publications (not already cited in Section 1)

Deumer, J., Schürmann, R., Gaál, A. et al. Traceable characterization of hollow organosilica beads as potential reference materials for extracellular vesicle measurements with optical techniques. *Discover Nano* 19, 14 (2024). <https://doi.org/10.1186/s11671-024-03956-3>

Carling RS, Barclay Z, Cantley N, Ghansah N, Hogg SL, Horman A, Moat SJ, Cowen S, Hopley C, Deaves C, Whyte E. Simple steps to achieve harmonisation and standardisation of dried blood spot phenylalanine measurements and facilitate consistent management of patients with phenylketonuria. *Clin Chem Lab Med*. 2025 Feb 4;63(7):1336-1343. doi: 10.1515/cclm-2024-1367. PMID: 39895045.

He HJ, He Z, et al. Interlaboratory assessment of candidate reference materials for lentiviral vector copy number and integration site measurements. *Mol Ther Methods Clin Dev*. 2025 Apr 21;33(2):101472. doi: 10.1016/j.omtm.2025.101472. PMID: 40621474; PMCID: PMC12229725.

Scott, S., Devonshire, A., Dillon, R. et al. Recommendations from the AML molecular MRD expert advisory board. *Leukemia* 38, 1638–1641 (2024). <https://doi.org/10.1038/s41375-024-02275-x>

Buchta, Christoph, et al. "Reference, calibration and referral laboratories – a look at current European provisions and beyond" *Clinical Chemistry and Laboratory Medicine (CCLM)*, vol. 63, no. 4, 2025, pp. 656-669. <https://doi.org/10.1515/cclm-2024-1066>

Jim F. Huggett, Denise M. O'Sullivan, et al. Ensuring accuracy in the development and application of nucleic acid amplification tests (NAATs) for infectious disease. *Molecular Aspects of Medicine*, Volume 97, <https://doi.org/10.1016/j.mam.2024.101275>.

Cleveland MH, He HJ, Milavec M, Bae YK, Vallone PM, Huggett JF. Digital PCR for the characterization of reference materials. *Mol Aspects Med*. 2024 Apr;96:101256. doi: 10.1016/j.mam.2024.101256. Epub 2024 Feb 14. PMID: 38359699.

Plebani M, et al. Point-of-care testing: state-of-the art and perspectives. *Clin Chem Lab Med*. 2024 Jun 17;63(1):35-51. doi: 10.1515/cclm-2024-0675. PMID: 38880779.

Campbell JJ, Almond N, Bae Y-K, Bhuller R, Briones A, Cho S-J, Cleveland MH, Cleveland TE IV, Galaway F, He H-J, et al. Standards and Metrology for Viral Vectors as Molecular Tools: Outcomes from a CCQM Workshop. *Biologics*. 2024; 4(2):187-201. <https://doi.org/10.3390/biologics4020013>

Stephen A Bustin, et al, MIQE 2.0: Revision of the Minimum Information for Publication of Quantitative Real-Time PCR Experiments Guidelines, *Clinical Chemistry*, Volume 71, Issue 6, June 2025, Pages 634–651, <https://doi.org/10.1093/clinchem/hvaf043>

Kammel M, et al. From crisis to routine - Standardization of SARS-CoV-2 genome detection by enhanced EQA schemes in a scientific pandemic network. *Int J Med Microbiol*. 2025 Jun;319:151656. doi: 10.1016/j.ijmm.2025.151656. Epub 2025 May 24. PMID: 40479806.

Devonshire, A.S., Morata, J., Jubin, C. et al. Interlaboratory evaluation of high molecular weight DNA extraction methods for long-read sequencing and structural variant analysis. *BMC Genomics* 26, 698 (2025). <https://doi.org/10.1186/s12864-025-11792-7>

Eloise J Busby, Leandro Lo Cascio, Violette Turon, Alexandra S Whale, Jim F Huggett, Alison S Devonshire, Next-Generation Methods for More Precise Measurement of Cancer Genetic Changes, *Clinical Chemistry*, Volume 71, Issue 7, July 2025, Pages 725–727, <https://doi.org/10.1093/clinchem/hvaf067>

Accurate quantification of carboplatin adducts with serum proteins by monolithic chromatography coupled to ICPMS with isotope dilution analysis. Raquel Larios et al., 2019. J. Anal. Atom. Spectrom., 34, 729-740. DOI: <https://doi.org/10.1039/C8JA00409A>

A species-specific double isotope dilution strategy for the accurate quantification of platinum–GG adducts in lung cells exposed to carboplatin. Susana Cuello-Nunez et al., 2017. J. Anal. Atom. Spectrom., 32, 1320-1330. DOI <https://doi.org/10.1039/C7JA00078B>

Presentations

- European digital PCR symposium and workshop 2024 ([eudip2024](#)), Ghent, Belgium. Feb 2024. NML at LGC took part in this event with an invited keynote lecture (Jim Huggett) and a poster presentation (Eloise Busby) titled “Benchmarking sepsis gene expression diagnostics using RNA-seq and RT-dPCR”.titled “Benchmarking sepsis gene expression diagnostics using RNA-seq and RT-dPCR”.
- European digital PCR symposium and workshop 2025 ([eudip2025](#)), Ghent, Belgium. November 2025. NML at LGC took part in this event with an invited keynote lecture (Jim Huggett) and a selected oral presentation (Dilek Yener) titled “Multiplexed dPCR Reference Gene Measurement for Genomic and Cell-Free DNA analysis”.
- AD-PD conference, Vienna, April 2025. AD-PD conference is one of the largest international gatherings dedicated to Alzheimer’s Disease (AD) and Parkinson’s Disease (PD). NML at LGC participated with a poster presentation, titled “Quantification of NfL in cerebrospinal fluid by mass spectrometry: Towards implementation of a reference measurement procedure.”
- ESCMID Global (35th Congress of the European Society of Clinical Microbiology and Infectious Diseases), April 2025. Presentation titled “Approach to measuring efficiency of pooled molecular tests”, NML at LGC highlighted the issues around quality assessment for pooled PCR testing, using COVID-19 as a model.
- IFCC Satellite Symposium, EuroMedLab 2025, Brussels, May 2025. The event brought together internationally renowned speakers to explore the role, methodologies, and applications of mass spectrometry in laboratory medicine. NML at LGC participated with a presentation titled “Role of mass spectrometry in the standardisation of protein biomarker measurements”.
- Solutions in Science (SinS), July 2025. NML at LGC participated with a poster presentation titled “Toward standardisation in clinical diagnostics: Investigations into liquid handling robotics to underpin SI traceable value assignment for multiple analytes”.
- 47th Meeting of the International Society for Biomarkers in Oncology (ISOBM), Murnau, Germany, October 2025. Alison Devonshire presented on “The GenomeMET project: approaches for standardization of liquid biopsy and genomic profiling methods”.
- 2025 Annual Academic Conference of the Clinical Medicine Committee of the Chinese Society of Biochemistry and Molecular Biology & 3rd Purple Mountain International Forum on Clinical Molecular Diagnostics, November 2025. Carole Foy presented on “Standards and metrology to support cancer genomic profiling”.
- The Association for Mass Spectrometry & Advances in the Clinical Lab (MSACL), September 2025. NML at LGC presented a poster titled “Standardisation and harmonisation of clinical measurements: A case study in phenylketonuria (PKU) monitoring”

4. Reference laboratory networks /collaborations focusing on developing /implementing reference measurement systems

(Please describe your participation in laboratory networks, forums or professional/technical committees linked to reference measurements system development/implementation, and contributions to JCTLM Working Group activities.)

IFCC activities

- Chair IFCC-WG-NP (natriuretic peptides)
- Co-Chair IFCC-WG-BND (Biomarkers of Neurodegenerative Diseases, with focus on neurofilament light chain)
- Chair of the Committee on Molecular Diagnostics in Infectious Diseases (C-MDID)
- Membership of Committee on Molecular Diagnostics in Oncology (C-MDO)

ISO/TC 212 Medical laboratories and *in vitro* diagnostic systems

- ISO/TC 212/WG 2 Reference systems (UK representation)
- ISO/TC 212/WG 4 Microbiology and molecular diagnostics (Expert)
- ISO/TC 212/JWG6 Joint ISO/TC 212 - ISO/TC 276 WG: Quality practice for detection of SARS-CoV-2
- Engaging with the activities within this ISO committee included drafting new or revision of existing standards:
 - o ISO/WD TS 8219 - Sequencing and clinical application to infectious diseases (new)
 - o ISO/FDIS 18704 - Molecular *in vitro* diagnostic examinations — Requirements and recommendations for pre-examination processes for urine and other body fluids — Isolated cell-free DNA (new)
 - o ISO/FDIS 15193 - *In vitro* diagnostic medical devices — Requirements for reference measurement procedures
 - o ISO/FDIS 15194 - *In vitro* diagnostic medical devices — Requirements for certified reference materials and the content of supporting documentation

ISO/TC 276 Biotechnology

- ISO/TC 276/SC1/WG 1 Analytical methods / Gene delivery
- ISO/TC 276/SC1/WG 2 Cell characterisation
- ISO/TC 276/SC1/WG 3 Analytical methods / Nucleic acids characterisation
- ISO//TC 276/WG4 Bioprocessing for cells and related entities
- ISO//TC 276/WG6 Nucleic acid- and protein-based devices
- Engaging with the activities within this ISO committee included drafting new or revision of existing standards:
 - o ISO/FDIS 16921-1 - Biotechnology — Gene delivery systems — Part 1: Vocabulary (new)
 - o ISO/DIS 16921-2 - Biotechnology — Gene delivery systems — Part 2: Guide for methods for the qualification of viral vectors (new)
 - o ISO/DIS 16921-2 - Biotechnology — Requirements for RNA quantification methods for gene expression analysis of biological and bioengineered systems (new)
 - o ISO/DIS 8934-1 - Biotechnology — Cell viability analytical methods Part 1: General requirements and considerations (new)
 - o ISO/DIS 23511 - Biotechnology — General requirements and considerations for cell line identification and cross-contamination testing
 - o ISO/DIS 20391-1 - Biotechnology — Cell counting - Part 1: General guidance on cell counting methods
 - o ISO/AWI 20395 - Biotechnology — Requirements for evaluating the performance of quantification methods for nucleic acid target sequences — qPCR and dPCR
 - o ISO/AWI 16921-3 - Biotechnology — Gene delivery systems Part 3: Guide for Methods for the Quantification and Characterization of Lipid Nanoparticles (new)

CEN/TC 140 *In vitro* diagnostic medical devices

- CEN/TC 140/WG 3 Quality management in the medical laboratory

Metrology committees and networks

- Representation in CCQM-Cell (Chair), Protein, Nucleic Acids (Chair), Organic and Inorganic Analysis Working Groups (CAWG, PAWG, NAWG, OAWG, IAWG)
- European Metrology Network on Traceability of Laboratory Medicine (EMN TLM) (Secretary)

JCTLM WGs

- Vice Chair (Analyte Group 2), JCTLM DBWG
- Nucleic acid review team leader (JCTLM DBWG)
- Acting Haemostasis review team leader (JCTLM DBWG)

Other societies and consortia

- International Society for Advancement in Cytometry (ISAC)- Innovation Committee member
- European Partnerships in Metrology project consortia: CoMET, NEuroBioStand, ProMET, GenomeMET
- European Liquid Biopsy Society
- Northern EV (Extracellular Vesicle) Network (UK)
- European Technology Platform for Nanomedicines

5. Open questions and suggestions to be addressed by JCTLM

(Suggestions on issues related to standardization and metrological traceability that should be considered by the JCTLM)

Note: The information of this report will be accessible publicly on the relevant JCTLM Members webpage, unless the author of the report states otherwise. In the case the organization does not authorize the publication of the report in part or full, the author will add a statement to clarify which part(s) of the report will /will not be rendered public.