

Draft template for biennial activity report from JCTLM Member organisations

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. Organisations are invited to provide the information below for submission to the Executive Committee.

Organisation Name: Health Sciences Authority (HSA), Singapore

JCTLM Member status: National and Regional Member

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Period covered: 2024 – 2025

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

(Please describe what activities your organisation 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.)

▪ Accuracy-Based External Quality Assessment (EQA) Programmes

HSA continues to organise accuracy-based EQA programmes for local clinical laboratories and medical clinics in Singapore, where metrologically traceable assigned (target) values determined by the Chemical Metrology Laboratory (CML) are used to evaluate the results of the participating laboratories/clinics.

HSA EQA Programme on HbA1c Testing

The HSA EQA Programme on HbA1c Testing is a mandatory programme for licensed hospitals, medical clinics and clinical laboratories which offer HbA1c testing for the diagnosis of diabetes mellitus. The programme comprises three cycles per year and two blood samples with different levels of HbA1c are provided in each cycle. Sixty-seven clinical laboratories and medical clinics participated in each cycle of the EQA Programme in 2025, reflecting a 6% increase in participation compared to 2023.

HSA EQA Programme in Clinical Chemistry

The HSA EQA programme for clinical laboratories is an on-going programme launched since 2011. The programme is intended to focus on chronic diseases affecting majority of the Singapore population. Starting from 2024, a new analyte, vitamin D metabolites in serum, was included in this EQA programme. In total, 18 Clinical markers are offered in this programme. The analytes include:

- (a) creatinine, glucose, total cholesterol, triglycerides (as 'total glycerides'), urea, uric acid, LDL-cholesterol, HDL-cholesterol, total protein, calcium, sodium, potassium, magnesium, iron, chloride, and vitamin D metabolites in human serum; and
- (b) albumin and creatinine in human urine.

This programme comprises two cycles per year. Four serum samples and one urine sample are provided in each cycle. Close to 40 clinical laboratories in Singapore participated in this EQA programme. Over the years, the results were continuously analysed to identify any trends. In view of the continued high prevalence of diabetes among the Singapore population, HSA will further customise the EQA programmes to study biases between different methods and/or analysers where samples from diabetics pose a concern to the accuracy of measurements of other clinical markers.

HSA PT scheme for determination of electrolytes in dialysate

The HSA PT scheme for determination of electrolytes in dialysate is a programme designed to support the quality assurance requirements for outpatient renal centres in Singapore. Under the Healthcare Services (Outpatient Renal Dialysis Service) Regulations 2023, outpatient renal centres must comply with stringent testing requirements, whereby the testing of electrolytes in dialysate must be conducted by laboratories accredited by the Singapore Accreditation Council, with regulatory accuracy requirements of $\pm 3\%$ for sodium and $\pm 5\%$ for potassium, calcium, magnesium, bicarbonate and chloride of the labelled concentration. This PT scheme provided dialysate samples to participating laboratories for analysis of the critical electrolyte parameters. The scheme ensures that outpatient renal centres are supported by capable testing laboratories that can meet the regulatory standards essential for patient safety in dialysis treatment.

▪ **Clinical Certified Reference Materials (CRMs) Maintained / Produced / Under Development**

HSA continues to maintain the following clinical CRMs through regular stability testing:

- (a) HRM-3002B: Creatinine, glucose, total cholesterol, HDL-cholesterol, LDL-cholesterol, total glycerides, free glycerol, urea and uric acid in human serum
- (b) HRM-3003B: Haemoglobin A1c in human blood
- (c) HRM-3004A: Albumin and creatinine in human urine
- (d) HRM-2002A: Calcium, potassium and sodium in human serum
- (e) HRM-2005A: Calcium, iron, potassium, magnesium, sodium and chloride in human serum
- (f) HRM-2011A: Sodium, chloride, copper, selenium and phosphorus in human serum
- (g) HRM-1016A: Carbamazepine
- (h) HRM-1027A: Sibutramine hydrochloride monohydrate
- (i) HRM-3005A: Cortisol in human serum
- (j) HRM-3006A: Testosterone in human serum
- (k) HRM-3007A: Creatinine, glucose, urea and uric acid in human serum
- (l) HRM-3008A: Total cholesterol, triglycerides, HDL-cholesterol, and LDL-cholesterol in human serum
- (m) HRM-3010A: Glycated VHLTPE peptide solution (in conjunction with HRM-3011A as the calibrant for the determination of the amount-of-substance fraction of haemoglobin A1c)
- (n) HRM-3011A: VELTPE peptide solution (in conjunction with HRM-3010A as the calibrant for the determination of the amount-of-substance fraction of haemoglobin A1c)

HSA produced the following clinical CRM between 2024 - 2025:

- (a) HRM-3009A: Human albumin solution
- (b) HRM-3013A: Albumin in human urine (five levels with wide concentration range)

Certification of the following clinical CRMs is in progress:

- (a) HRM-3014A: Human albumin solution for total protein measurement

Commutability study:

Commutability studies on albumin in urine CRM (HRM-3013A) were completed in 2025. The studies involved HSA, three clinical laboratories within public hospitals and a major private clinical laboratory in Singapore.

JCTLM listing:

The following CRMs were approved for listing in the JCTLM Database in 2024-2025:

- (a) HRM-3004A Albumin and creatinine in human urine
- (b) HRM-1027A Sibutramine hydrochloride monohydrate

The following CRM was nominated for listing in the JCTLM Database in 2025:

- (a) HRM-3013A Albumin in human urine

▪ **Reference Measurement Methods Developed / in Development**

- (a) LC-IDMS/MS method for 17 β -estradiol in human serum (method revalidated for very low concentration for participation in CCQM Key Comparison)
- (b) High resolution IDMS method for human growth hormone in human serum
- (c) LC-MS/MS and LC-UV methods for the purity assessment of parathyroid hormone
- (d) Ion chromatography methods for phosphate in human serum
- (e) LC-IDMS/MS method for cystatin C in human serum (in progress)
- (f) GC-MS method for bicarbonate in human serum (in progress)
- (g) LC-IDMS/MS method for virus spike protein in cell culture (in progress)

JCTLM Listing:

The following RMP was nominated for listing in the JCTLM Database in 2025:

- (a) LC-IDMS/MS reference measurement procedure for albumin in urine (Supporting publication: Clin Chem Lab Med 2021;59(4):711-720)

▪ **International Comparisons Related to Healthcare Co-organised / Participated**

HSA co-organised the following comparisons:

- (a) CCQM-P219 Pilot study on determination of the amount-of-substance fraction of [Hb1c/(HbA1c+HbA0)] in human hemolysate
- (b) CCQM Task group comparison on standardisation of IDMS method for HbA1c
- (c) NIDDK round robin on standardisation of reference measurement procedures for urine albumin
- (d) CCQM-K195/P253 Determination of of the amount-of-substance fraction of [Hb1c/(HbA1c+HbA0)] in human hemolysate (in progress)

HSA participated in the following comparisons:

- (a) CCQM-P232 Fire drill influenza RNA copy number quantification
- (b) 2024 IFCC RELA on HbA1c
- (c) CCQM-115.d Recombinant, cross-links-free protein in solution: Mass fraction of Parathyroid hormone 1-84 in aqueous solution (in progress)
- (d) CCQM-192 17 β -Estradiol in human serum (in progress)
- (e) CCQM-P244 Lipid Nanoparticles with Encapsulated RNA (in progress)

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

(Please outline R&D project(s) and/or programme(s) planned by your organisation in the next two years including information on: new measurement area(s)/meaurands of interest for your organisation; 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.)

▪ **Development of Clinical CRMs**

- (a) Vitamin D metabolites in human serum
- (b) Steroid hormones (progesterone and estradiol) in human serum
- (c) HbA1c in human blood (replacement batch)
- (d) Cystatin C in human serum

▪ **Method development**

- (a) Aldosterone in human serum

- (b) 1,25-Dihydroxyvitamin D3 and D2 in human serum

3. Promoting traceability in laboratory medicine

(Please describe activities your organisation 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 Related to Healthcare

- (a) Extent of Equivalence of Results for Urine Albumin among 3 Candidate Mass Spectrometry Reference Measurement Procedures

Miller WG, Bachmann LM, Budd J, Beasley-Green A, Phinney KW, Tan HT, et al. Clin Chem 2024;70(11):1375-1382.

This research paper addresses a critical need in the standardisation of urine albumin measurement, an essential biomarker for the diagnosis and management of chronic kidney disease. Despite its clinical importance, current in vitro diagnostic medical devices show substantial variability in urine albumin results, which can lead to inconsistent interpretation and challenges in patient care. Establishing higher-order reference measurement procedures (RMPs) is therefore necessary to ensure metrological traceability and harmonisation across testing platforms. This study evaluates the comparability of three candidate mass spectrometry-based RMPs and demonstrates that they achieve a suitable level of agreement and measurement uncertainty. The confirmation of their equivalence provides a foundational step toward implementing standardised urine albumin measurement globally, supporting more reliable clinical decisions and improving patient outcomes.

- (b) Expedient measurement of total protein in human serum and plasma via the biuret method using fiber optic probe for patient samples and certified reference materials

Yong S, Ng CY, Liu H, Chen Y, Liu Q, Teo TL, et al. Anal Bioanal Chem 2024;416:6611-6620.

This research paper presents a streamlined and reliable approach for measuring total protein in human serum and plasma using the biuret method with a fiber optic probe. Accurate determination of total protein is essential in clinical diagnostics, and the biuret method is recognised by JCTLM as a reference measurement procedure. However, achieving high precision and trueness requires strictly controlled and consistent measurement conditions, which can be challenging with conventional cuvette-based workflows due to the time-dependent nature of the biuret reaction. By employing a fiber optic probe, this study demonstrates a faster and simpler measurement process that maintains analytical quality while improving operational efficiency. The method showed excellent agreement with certified reference materials and clinical analyzer results, supporting its suitability as a practical candidate reference method. These findings are significant because they offer a more convenient and robust approach to ensuring accurate total protein measurement, which is fundamental for reliable clinical decision-making and laboratory standardisation.

- (c) A comparison of fetal hemoglobin interference in routine high-performance liquid chromatography, immunoassay, and enzymatic methods of glycated hemoglobin measurement

Soh SX, Loh TP, Liu Q, Liu H, Tjai M, Tan HW, et al. Lab Med 2025;56(4):402-406.

This research paper addresses the clinically important challenge of fetal haemoglobin (HbF) interference in the measurement of glycated haemoglobin A1c (HbA1c), a key marker used to diagnose and monitor diabetes. Because different analytical platforms vary in their response to HbF, inaccurate HbA1c results can occur in patients with elevated HbF levels, including pregnant individuals, patients with haemoglobinopathies, and newborns. However, existing data on the extent of HbF interference are incomplete or unavailable for several commonly used laboratory systems. By systematically evaluating

seven HbA1c measurement platforms across a wide range of HbF concentrations using isotope dilution mass spectrometry as a reference, this study provides essential performance evidence that clarifies which methods remain reliable and which may yield clinically significant error. The findings have direct implications for laboratory method selection and patient result interpretation, supporting more accurate diabetes assessment in individuals with elevated HbF.

- (d) Advancing accuracy in chronic kidney disease diagnosis and management: reference materials and reference measurement procedures for clinical markers
Tan HT, Liu Q, Teo TL. *Ann Lab Med* 2025;45:367-380.

This review article highlights the critical role of measurement standardisation in improving the diagnosis and management of chronic kidney disease (CKD). As CKD continues to rise globally due to increasing rates of diabetes, obesity, and hypertension, clinical laboratories are under growing pressure to provide accurate and comparable results for key biomarkers that guide patient care. However, measurement inconsistencies across different testing platforms and regions remain a major barrier to reliable clinical decision-making. By examining the development and application of reference materials (RMs) and reference measurement procedures (RMPs) for core CKD biomarkers including creatinine, urine albumin, cystatin C, and urea, this review underscores how standardisation efforts can enhance diagnostic accuracy, enable more meaningful disease monitoring, and ultimately support better health outcomes. Ensuring harmonised laboratory measurements is therefore not only a technical necessity, but also a foundational element in global strategies aimed at reducing morbidity, mortality, and healthcare burden related with CKD.

▪ **Presentations/Seminars Related to Healthcare**

- (a) 2024 HSA EQA Programme Symposium for participating clinical laboratories of EQA programme, March 2024.
- (b) “Independent assessment of six commercial methods for Hemoglobin A1c in the presence of Hemoglobin E”, Sharon Yong, invited presentation at APMP Medical Metrology Focus Group Workshop, August 2024.
- (c) “Case Study: Organising Accuracy-Based EQA Programmes and Its Impact on Regulation”, Qinde Liu, invited webinar for APMP TCQM Webinar: Metrology and Its Impact to the Clinical Laboratory Community, September 2024.
- (d) “HSA Chemical Metrology Laboratory’s Journey in External Quality Assessment”, Tang Lin Teo, invited presentation at Singapore General Hospital ClinPath FiT Workshop, Singapore, October 2024.
- (e) 2025 HSA EQA Programme Symposium for participating clinical laboratories of EQA programme, March 2025.
- (f) “Metrological Services for Clinical Measurements: Reference Measurement Procedure, Reference Material and Accuracy-Based External Quality Assessment Programme”, Qinde Liu, invited presentation at APEC Workshop on Measurement of Clinical Markers for Non-Communicable Diseases, Singapore, April 2025.
- (g) “Impact of Metrology in Supporting Healthcare – The Singapore’s Story”, Hwee Tong, poster with audio presentation at World Metrology Day Symposium - 150 Years of the Metre Convention: Science, Innovation and Global Impact, Paris, France, May 2025.
- (h) “Standardisation of Urine Albumin Assay: Development of Reference Measurement Procedure and Reference Materials”, Qinde Liu, invited keynote presentation at Beijing Conference and Exhibition on Instrumental Analysis, September 2025.

- (i) “Accuracy-Based External Quality Assessment Programme” and “Evaluation of Measurement Uncertainty Using EQAP Results”, Qinde Liu, Presentations at Stakeholder Engagement Session on Accuracy-Based External Quality Assessment Programme, Kular Lumpur, Malaysia.
- (j) “HbA1c Hexapeptide CRMs: Development Insights and Applications”, Sharon Yong, Invited presentation at APMP TCQM Workshop, November 2025.

- **Courses for Healthcare Sector**

- (a) Onsite training course on measurement uncertainty for clinical laboratories for local clinical labs in October 2024.
- (b) Onsite training course on Measurement uncertainty related to clinical applications for a clinical laboratory in Brunei Darussalam in November 2024.
- (c) Self-directed online training on measurement uncertainty for clinical laboratories (available all time).

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.)

- Five HSA staff members are currently serving in the JCTLM Database Working Group:

- (a) Dr Qinde Liu
Vice-Chair of Analyte Group 1
Team Leader of Non-Peptides Hormones Review Team
Member of Metabolites and Substrates Review Team
- (b) Dr Richard Shin
Member of Non-Electrolyte Metals Review Team
- (c) Dr Hwee Tong Tan
Member of Proteins Review Team
- (d) Ms Hong Liu
Member of Vitamins and Micronutrients
- (e) Dr Fransiska Dewi
Member of Electrolyte and Blood Gases

- **NIDDK Urine Albumin Standardisation Programme**

In collaboration with NIST, the University of Minnesota, and the Mayo Clinic, the round robin comparison for standardisation of reference measurement procedures for urine albumin has been successfully completed. The results demonstrated good agreement among the three reference laboratories, confirming the successful standardisation of the procedures. Following this achievement, NIDDK has proposed that calibration of IVD manufacturers’ assays be standardised using the JCTLM-listed reference measurement procedures for urine albumin by 2027.

- **Collaboration with US CDC**

- (a) HSA continued its collaboration with the US CDC on the measurement of LDL-cholesterol and HDL-cholesterol in human serum. The evaluation of the beta-quantification (BQ) reference measurement procedure for LDL-cholesterol has been completed. Building on this work, the collaboration has now progressed to a comparative study between the IDMS and Abel–Kendall methods, with the objective of transitioning the LDL-cholesterol reference measurement system to a more accurate and precise IDMS-based approach. The outcomes of this collaboration are expected to strengthen global traceability and

reliability of cholesterol testing, thereby supporting improved cardiovascular risk assessment and clinical decision-making.

- (b) HSA and CDC have planned to carry out a collaborative project on evaluating the performance of point-of-care devices for lipid testing, including total-cholesterol, LDL-cholesterol, HDL-cholesterol, and triglycerides.

5. Open questions and suggestions to be addressed by JCTLM

(Suggestions on issues related to standardisation 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 organisation does not authorise 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.