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: Health Sciences Authority, Singapore

JCTLM Member status: Member

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Period covered: 2018 – 2019

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.)

- **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. In 2019, a dedicated EQA programme on HbA1c Testing is launched along with the regular EQA programme.

  **The HSA EQA Programme on HbA1c Testing**

  In March 2019, Singapore’s Ministry of Health mandated that all licensed hospitals, medical clinics and clinical laboratories intending to offer HbA1c as an alternative screening test (other test being fasting plasma glucose) for diabetes mellitus are required to participate in the HSA EQA programme. The use of HbA1c as a screening tool offers the ability to diagnose patients with diabetes mellitus even with non-fasted blood samples. With the potential for increased use of HbA1c testing, HSA offers the EQA programme as a continuous quality assurance programme to assist laboratories/clinics in tightening the accuracy of their HbA1c test results, and reducing the possibilities of misclassification of diabetes mellitus. This programme is amenable to both mainframe analysers and portable devices as fresh human whole blood samples are provided for testing. The programme comprises three cycles, where two blood samples with different HbA1c levels are provided per cycle. In the 2019 programme, a total of 59 clinical laboratories and medical clinics participated in the programme.

  **Regular HSA EQA Programme on Clinical Chemistry**

  The regular 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, being diabetes and lipid order. 16 Analytes are offered in this programme, which comprises two cycles. The analytes include:
(a) creatinine, glucose, total cholesterol, triglycerides (as ‘total glycerides’), urea, uric acid, LDL-cholesterol, HDL-cholesterol, calcium, sodium, potassium, magnesium, iron, and chloride in human serum; and
(b) albumin and creatinine in human urine.

A total of 47 and 41 clinical laboratories, including all public and almost all private laboratories, participated in the regular HSA EQA programme in 2018 and 2019, respectively. The reduction in the number of participating laboratories in 2019 was attributed to laboratories which only test for HbA1c and therefore participated in the dedicated HSA EQA Programme on HbA1c Testing only.

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

  HSA continues to maintain the following clinical CRMs:
  (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-2005A: Calcium, iron, potassium, magnesium, sodium and chloride in human serum
  (e) HRM-2011A: Sodium, chloride, copper, selenium and phosphorus in human serum

  HSA has produced the following clinical CRMs in 2018 - 2019:
  (a) HRM-3005A: Cortisol in human serum

  A new clinical CRM, HRM-3006A: Testosterone in human serum is expected to be ready by March 2020.

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

  (a) LC-IDMS\(^3\) method for human growth hormone in human serum
  (b) LC-IDMS/MS method for the determination of concentration of insulin solution
  (c) LC-IDMS/MS method for the determination of concentration of amino acids solution
  (d) Spectrophotometry method for total protein in human serum (in progress)
  (e) LC-IDMS/MS method for amino acids in human serum (in progress)

- **CCQM Comparisons Related to Healthcare Co-organised / Participated**

  HSA co-organised the following comparisons:
  (a) CCQM-K115.c Peptide purity: HbA1c glycated hexa-peptide, GE (in progress)
  (b) CCQM-K115.2018 Peptide purity: HbA1c hexa-peptide, VE (in progress)

  HSA participated in the following comparisons:
  (a) CCQM-K151 & CCQM P191 Key comparison and pilot study on protein quantification: synthetic insulin analogue
  (b) 2018 IFCC RELA on HbA1c in human haemolysate
  (c) 2018 IFCC RELA on total glycerides in human serum
  (d) 2018 IFCC RELA on calcium in human serum

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)/meaurands 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.)

- **Expansion of HSA EQA Programme**

  Total protein in human serum will be included in the regular HSA EQA programme in 2020.

- **Development of Reference Measurement Methods**

  (a) LC-IDMS/MS method for estradiol in human serum  
  (b) Spectrophotometric method for total protein in human serum

- **Development of Clinical CRMs**

  (a) Vitamin D metabolites in human serum  
  (b) Steroid hormones (progesterone and estradiol) in human serum  
  (c) Human albumin solution calibration standard

- **Other Activities**

  (a) Implemented our reference method for HbA1c in the measurement of blood samples with haemoglobin variants (HbE and HbD) in collaboration with two local public hospital laboratories. With positive initial results, we will expand our pool of samples to conduct further measurements.  
  (b) Continued to implement our beta-quantification method in the collaboration with United State’s Centers for Disease Control and Prevention (CDC) on the measurement of HDL-cholesterol and LDL-cholesterol, and investigation on the impact of ultra-centrifugation procedure.  
  (c) Conducted a survey on the performance of point-of-care devices (POC) from suppliers. Initial results showed that the POC devices were not comparable to mainframe analysers in public hospital laboratories. With a demand for faster results, improvements in POC devices for lipid testing are anticipated. In view of this, further survey will be carried out in another 2 to 3 years.

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 Related to Healthcare**

  (a) Commutable whole blood reference materials for hemoglobin A1c validated on multiple clinical analyzers  

  (b) Simple and accurate candidate reference measurement procedure for total testosterone in human serum by one-step liquid-liquid extraction coupled with isotope dilution mass spectrometry  
    Chen YZ, Teo HL, Liu H, Loh TP, Liu Q, Teo TL, Lee TK, Sethi SK. Analytical and Bioanalytical Chemistry, Accepted for publication.

  (c) Enhancing the accuracy of measurement of small molecule organic biomarkers

- **Presentations/Seminars Related to Healthcare**

(a) 2017 HSA EQA Programme Symposium for participating clinical laboratories of HSA EQA programme, January 2018.

(b) “HSA External Quality Assessment Programme – An Accuracy-Based EQA Programme”, Liu Qinde, oral presentation at SACB Education Programme 2018, September 2018.


(d) “HbA1c Measurement by IDMS – Current Situation and Future Development”, Liu Qinde, oral presentation at Protein and Peptide Therapeutics and Diagnostics (PPTD): Research and Quality Assurance International Workshop, Chengdu, October 2018

(e) “Establishing Metrological Traceability in Clinical Measurements – the Singapore Experience”, Liu Qinde, oral presentation at 14th Annual National Symposium on Reference Systems in Laboratory Medicine, Shanghai, November 2018.

(f) 2018 HSA EQA Programme Symposium for participating clinical laboratories of HSA EQA programme, February 2019.

(g) MOH-HSA Joint Dialogue Session with Clinical Laboratories on External Quality Assessment for HbA1c Testing, April 2019.


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.)

- **JCTLM**

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

(1) Dr Qinde Liu  
Vice-Chair of Analyte Group 1  
Team Leader of Non-Peptides Hormones Review Team  
Member of Metabolites and Substrates Review Team

(2) Dr Richard Shin  
Member of Non-Electrolyte Metals Review Team
IFCC Standardization of Procalcitonin Assay (WG-PCT)

As a member of IFCC WG-PCT, HSA is collaborating with LNE, France on the development of LC-IDMS/MS method for the measurement of procalcitonin in human serum and purity determination of procalcitonin calibration standard. The target is to establish an IDMS-based reference method for procalcitonin in human serum, and to develop procalcitonin calibration standard and human serum CRM for the standardisation of procalcitonin assay.

In July – August 2019, HSA hosted a visiting PhD student from LNE for the method development of procalcitonin in human serum.

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)

   NIL

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 authorizes 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.