

## 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.

**Organisation:** Physikalisch-Technische Bundesanstalt (PTB)

**JCTLM Member status:** Ordinary Member

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**Period covered:** 2015 – 2017

### 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.)

PTB in close collaboration with the German Medical Council (Bundesärztekammer) already has a well-established and maintained national reference measurement system in laboratory medicine in Germany fulfilling legal requirements based on the German law for medical products (Medizinproduktegesetz-MPG). The MPG is the national implementation of EU IVD-Directive which is now replaced by (EU) 2017/746 regulation of the European Parliament and the European Commission from 5 April 2017 on *In-vitro*-Diagnostics.

The established infrastructure comprises accredited calibration laboratories that in turn monitor the performance of thousands of testing laboratories in laboratory medicine in Germany in accordance with the legal requirements for measurement quality.

#### Development of reference measurement procedures:

PTB has initiated and carried out a laboratory comparison on the determination of total Hemoglobin (Hb) in blood within the EMRP project HLT05. The equivalence of the results obtained from different MS-based techniques, Spectrophotometry and Raman Spectrometry was demonstrated.

PTB has initiated and is leading a CCQM Pilot Study (P164) on measuring the mass fraction human growth hormone in serum.

PTB has developed an ID-MS reference method for determination of the HBA2 fraction in hemoglobin. This is one of the key elements to promote the standardization of hemoglobin A2 measurement through the definition of an international reference system.

Established calibration (reference) measurement services:

Mass fraction of Selenomethionine in blood serum (BIPM CMC database entry: ptb-qm-w-020)

Mass fraction of Superoxiddismutase in blood serum.

Mass fraction of Hemoglobin in blood

Scientific publications:

Frank, C., Brauckmann, C.; Palos, M.; Arsene, C.G.; Neukammer, J.; Del Castillo Busto, M.E.; Zakel, S.; Swart, C.; Güttler, B.; Stosch, R.: Comparison of potential higher order reference methods for total hemoglobin quantification-an interlaboratory study. *Analytical and Bioanalytical Chemistry* (2017) 409, 2341-2351.

Paleari, R.; Caruso, D.; Kaiser, P.; Arsene, C.; Schaeffer-Reiss, C.; Van Dorsselaer, A.; Bisse, E.; Ospina, M.; De Jesús, V.R.; Wild, B; Mosca, A.: Developing a reference system for the IFCC standardization of HbA2. *Clinica Chimica Acta* (2016), 467, 21-26.

Arsene, C., Kaiser, P., Paleari, R., Henrion, A., Mosca, A., Candidate reference measurement procedure for determination of HbA2 by peptide mapping and isotope dilution mass spectrometry. *Analytica Chimica Acta*, submitted.

Brauckmann, C.; Frank, C.; Schulze, D.; Kaiser, P.; Stosch, R.; Swart, C.: Preparation and characterisation of an <sup>57</sup>Fe enriched hemoglobin spike material for species-specific isotope dilution mass spectrometry. *Journal of Analytical Atomic Spectrometry* (2016) 31, 1846-1857.

Gleitzmann, J.; Raab, A.; Schulze, D.; Wätzig, H.; Feldmann, J.; Swart, C.: Accurate and precise quantification of Cu, Zn-SOD in human red blood cells using species-specific double and triple IDMS. *Journal of Analytical Atomic Spectrometry* (2016) 31, 1922-1928.

Swart, C. and Jakubowski, N.: Update on the status of metrology for metalloproteins. *Journal of Analytical Atomic Spectrometry* (2016) 31, 1756-1765.

González Antuna, A., Rodríguez-González, P., Ohlendorf, R., Henrion, A., Delatour, V., García Alonso, J.I., Determination of cystatin C in human serum by isotope dilution mass spectrometry using mass overlapping peptides. *Journal of Proteomics* (2015) 112, 141-155.

Güttler, B., Zakel, S., Wundrack, S., Stosch, R., Isotope-dilution surface enhanced Raman Spectroscopy (ID-SERS) – a tool for metrologically traceable reference measurements at the highest precision level and its application in clinical chemistry. Chapter 9, *Handbook of Enhanced Spectroscopy* (2016), 307-325.

Gleitzmann, Julia, Development of primary measurement procedures for the determination of Cu-containing proteins with clinical relevance, Technische Universität Braunschweig, PTB-Bericht: PTB-CP-9, <http://d-nb.info/1129374068>, ISBN: 978-3-95606-305-3

## 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.)

PTB has initiated and will be leading a CCQM Pilot study on quantification of total Haemoglobin in blood.

In the framework of the EMPIR Call 2018 (Health), PTB will submit a proposal on quantitative diagnostic methods for biomarkers of coronary heart diseases.

PTB will continue to promote the IFCC standardization program for HBA2 by developing a secondary certified reference material in cooperation with JRC.

## 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)

### Presentations:

Swart, C.; Köllensperger, G.; Goenaga-Infante, H.; Raab, A.: Importance of reference measurement procedures in diagnostic of Alzheimer's disease. Metallomics 2017: The 6th International Symposium on Metallomics, Vienna, Austria

Gleitzmann, J.; Wätzig, H.; Swart, C.: IDMS-based quantification of metal-containing proteins with clinical relevance. Metallomics 2017: The 6th International Symposium on Metallomics, Vienna, Austria

Henrion A: Protein ID-MS in Biomatrix, SIM-Workshop Biometrology: Protein Certified Reference Materials (CRM) and Metrological Methods, 27.-29. Juni 2017, Rio de Janeiro, (invited)

Frank, C.; Wundrack, S.; Schmidt, S.; Stosch, R.: SI-Traceable Tau Protein Quantification by Surface Enhanced Raman Spectrometry - A First Step Towards Reliable Diagnosis of Alzheimer's Disease. 14th International Conference on Nanosciences & Nanotechnologies (NN17), Thessaloniki, Greece

Henrion A: MS-basierte Proteinquantifizierung und Referenzmethodenentwicklung, 16. Jahrestagung Sektion Molekulare Diagnostik der DGKL (Deutsche Vereinte Gesellschaft für Klinische Chemie und Laboratoriumsmedizin e.V.), 17.-19. Mai 2017, Tutzing, Germany (invited)

Henrion A: Reference Measurements for Human Growth Hormone, BIPM-WADA Symposium on Standards and Metrology for Anti-Doping Analysis, 28./29. September 2016, Sèvres, France (invited)

Gleitzmann, J.; Wätzig, H.; Swart, C.: Quantification strategies for ceruloplasmin based on IDMS. BNASS 2016: The 18th Biennial National Atomic Spectroscopy Symposium, Liverpool, United Kingdom

Henrion A: Massenaufgelöste, isoform-selektive Quantifizierung von Wachstumshormon, 13. Anwendertreffen der DGKL-AG LC-MS/MS in der Labormedizin, 26./27. Oktober 2015, Bad Staffelstein, Germany

Stosch, R.: Traceability of measurands in clinical chemistry based on internationally recognised reference procedures (invited talk). 9th Senftenberg Innovation Forum on Multiparametric Analytics, 2016, Senftenberg, Germany (invited).

Arsene C., et al.: Candidate reference measurement procedure for the determination of HbA2-fraction in human blood using mass spectrometry, 14th International Symposium on Biological and Environmental Reference Materials (BERM 14), October 11-15, 2015, Maryland, USA

Swart, C., et al.: New approach for the development of candidate reference measurement procedures, JCTLM Members' and Stakeholders' Meeting, 30 November -1 December 2015, BIPM, Sevres, France.

#### **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.)

PTB is contributing to RELA - IFCC External Quality assessment schemes for Reference Laboratories in Laboratory Medicine on a regular basis by providing reference values for a selected group of measurands having the highest priority.

The development of reference measurement procedures for protein biomarkers is being carried out in close cooperation with INSTAND e. V.

##### JCTLM Review team memberships

André Henrion is leading the JCTLM review team on “Drugs”

Claudia Swart joined the JCTLM review team on “Proteins” (2016)

Rainer Stosch joined the JCTLM review team on “Non-Electrolyte Metals” (2017)

#### **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.