JCTLM
Accurate results for patient care

Database Newsletter

https://www.bipm.org/jctlm/ Issue 8 | April 2021

We wish all our readers health and strength as we all continue to operate and adapt our activities in the context of COVID-19 pandemic.

In this issue of the JCTLM Newsletter, we report on highlights from the last Executive meeting; the activities of the JCTLM TEP WG and TF-RMSI; new entries and current database content; and plans for the next JCTLM meetings in 2021. We also welcome the new JCTLM Chair.

1 Dr Greg Miller appointed Chair of the JCTLM

Dr Greg Miller has been appointed Chair of the JCTLM, taking over from Prof. Ian Young who recently completed his two-year term.

Dr Miller is a Professor in the Pathology Department at Virginia Commonwealth University where he serves as Co-director of Clinical Chemistry and Director of Pathology Information Systems. His professional interests and research have focused on standardization and harmonization of laboratory results, quality control and external quality assessment/ proficiency testing. His current professional activities include: Associate Editor of the journal Clinical Chemistry, Chair of the Working Group for Commutability in Metrological Traceability of the IFCC, Chair of the Laboratory Working Group of the National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health (US), a member of the Harmonization Oversight Group of the International Consortium for Harmonization of Clinical Laboratory Tests, a member of the US delegation to ISO Technical Committee 212 for Clinical Laboratory Testing and In Vitro Diagnostic Test Systems, and other work groups for clinical laboratory standards.

Most recently Dr Miller has been working with the JCTLM, IFCC, BIPM and ICHCLR to organize a joint workshop on 'Overcoming challenges to global standardization of clinical laboratory testing: reference materials and regulations', which will be held as a virtual meeting in December 2021.

Dr Greg Miller

2 Highlights from the 22nd Executive Committee meeting

The 22nd meeting of the Executive Committee of the JCTLM was held by teleconference on 3-4 December 2020. The Executive Committee convened for the last time under the Chairmanship of Prof. Ian Young whose term ended in December. He was thanked for his support to the JCTLM.

Changes in the JCTLM Executive Committee representatives
The Committee approved the Chairmanship of Dr Greg Miller, and the BIPM's continued role as the Secretariat for the JCTLM effective in February 2021.

Update of the JCTLM Database
The JCTLM Executive decided on the development of a new version of the JCTLM Database to benefit of a new web designed user interface with a contextual search facility and machine-readability.

JCTLM Review teams' membership
The 5-year review process for JCTLM Review teams' membership was successfully completed and resulted in the reappointment of 75 % of the review teams' members who were contacted and attracted new members appointed during the year. There are presently 60 experts contributing to the twelve JCTLM review teams.

Virtual meeting of the JCTLM Members and Stakeholders
The Committee decided that the next meeting of the JCTLM Members and Stakeholders would be held remotely in December 2021, noting the difficult situation surrounding COVID-19. A separate item on this meeting appears in this Newsletter.

New JCTLM Member organizations
The JCTLM Executive approved the JCTLM membership of the Uzbek National Institute of Metrology" State Enterprise (UzNIM) and two Reference Laboratories of Autobio Diagnostics Co., Ltd from Beijing and Zhengzhou, China. As of 30 March 2021, there are 60 JCTLM Member organizations.

See the full text of the 2020 JCTLM Executive Meeting report.

3 New entries in the JCTLM database - www.bipm.org/jctlm/

The JCTLM review process conducted in 2020 has resulted in seven new entries in the JCTLM Database for available higher-order certified reference materials, as well as eleven newly published reference measurement methods, and fourteen new measurement services delivered by reference laboratories. The new entries are listed below:

New entries for available Certified Reference Materials

Analyte Category	Analyte*	Matrix/Material
Enzymes	Pancreatic alpha-amylase	buffer
Metabolites and substrates	L-Valine L-Proline L-Leucine L-isoleucine L-Phenylalanine	High-purity material
Proteins	Standard Solutions for Measurement for Glycated Albumin (JSCC method)	Calibration solutions

*Complete information for each certified reference material entry can be retrieved by clicking on the Analyte name.

New entries for Reference Measurement Methods

Analyte Category	Reference Measurement Method *(JCTLM Identification Number*)*
Drugs	ID LC-MS/MS based candidate reference method for the quantification of immunosuppressive drugs in human whole blood (JCTLM C16RMP7R (cyclosporine A), C16RMP8R (everolimus), C16RMP9R (sirolimus),and C16RMP10R (tacrolimus)) Taibon J. et al., *Clin. Biochem.*, 2020, **82**, 73-84
Metabolites and Substrates	ID-LC-MS/MS Reference measurement method for **urea** in human serum (JCTLM C16RMP12R) Han L. et al, *Journal of Pharmaceutical and Biomedical Analysis*, 2019, **162**, 124-129
Non-peptide hormones	ID LC-MS/MS based candidate reference method for the quantification of **androstenedione** in human serum (JCTLM C16RMP6) Gradl K. et al., *Clinical Mass Spectrometry*, 2020, **16**, 1-10 ID-LC-MS/MS reference measurement procedure for **total testosterone** in human serum (JCTLM C17RMP2) Chen Y. et al, *Analytical and Bioanalytical Chemistry*, 2019, **411**(28), 7519-7528 ID-LC-MS/MS Reference measurement method for **estriol (non-conjugated)** in human serum (JCTLM C16RMP13R) Huang X. et al, *Analytical and Bioanalytical Chemistry*, 2018, **401**(24), 6257-6267 ID-LC-MS/MS Reference measurement method for **17β-estradiol** in human serum (JCTLM C17RMP7) Zhang Q. et al, *Microchemical Journal*, 2020, **152**, 104270
Nucleic acids	dPCR reference measurement method for **human cytomegalovirus** quantification (JCTLM C15RMP11R) Pavsic J. et al., *Anal Bioanal Chem*. 2016, **408**, 67-75; *Anal Bioanal Chem*. 2016, **408**, 107-121; *Anal Bioanal Chem*. 2017, **409**, 2601-2614
Proteins	Spectrophotometric reference measurement method for **total haemoglobin** (JCTLM C17RMP1) Grote-Koska D. et al, *Clinical Chemistry and Laboratory Medicine*, 2020, **58**(8), 1314-1321

*Complete information for each method entry can be retrieved by clicking on the JCTLM identification number.

New entries for Reference Measurement Laboratory Services

Analyte Category	Analyte*	Location of laboratory
Enzymes	Alanine aminotransferase (ALT) Aspartate aminotransferase (AST) Creatine kinase (CK) Lactate dehydrogenase (LDH) Gamma-glutamyltransferase (GGT) Alpha-amylase (AMY) Alkaline phosphatase (ALP)	China
Non-peptide hormones	17beta-Estradiol	China
Metabolites and substrates	Creatinine Urea Glucose	China
Proteins	Total Protein Total Haemoglobin	China Germany

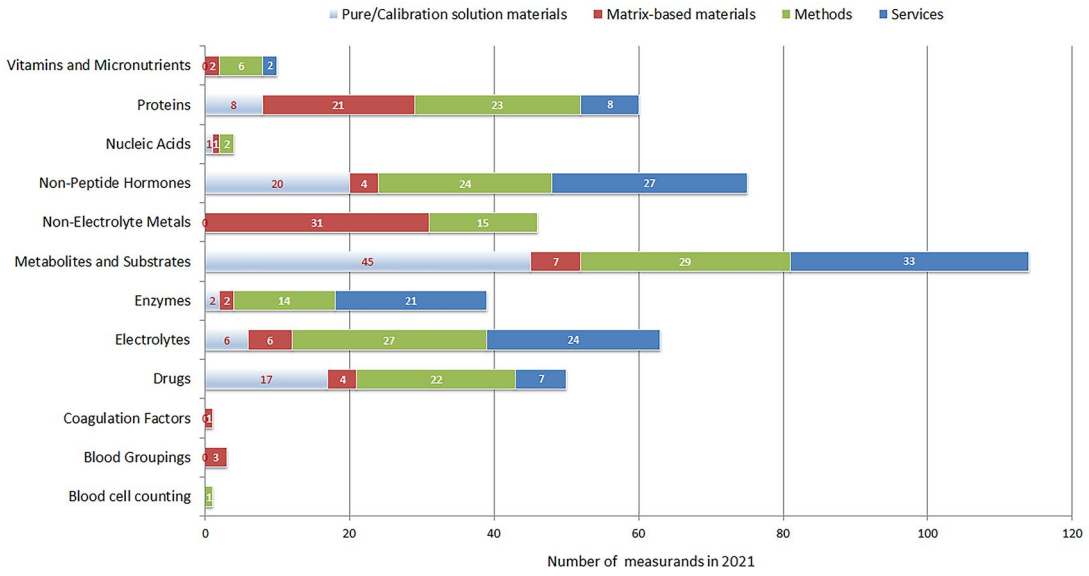
*Complete information for each reference measurement service can be retrieved by clicking on the Analyte name.

4 Content of the JCTLM Database

As of April 2021 the JCTLM Database contains:

- 257 entries of available higher order certified reference materials that represent 180 measurands in eleven categories of analytes.
- 213 reference measurement methods that represent 160 measurands in eight categories of analytes.
- 203 reference measurement services delivered by 18 reference laboratories and two national metrology institutes in seven countries and which represent 120 measurands in seven categories of analytes.

The bar chart below shows the distribution of the measurands for each type of analytes.



5 2021 Call for nominations

The JCTLM invites producers of materials, authors of method publications, and calibration laboratories that provide reference measurement services in laboratory medicine to submit nominations for review and possible inclusion in the JCTLM database.

Submissions should be sent to jctlm(a)bipm.org no later than 31 May 2021 using the procedures and forms available at: https://www.bipm.org/en/committees/jc/jctlm/jctlm-nominations-and-review.html

6 Activities of the JCTLM Working Group for Traceability, Education and Promotion

By Elvar Theodorsson JCTLM Working Group for Traceability, Education and Promotion (JCTLM WG TEP) Chair.

Elvar Theodorsson

The aim of WG-TEP is to produce and promote educational materials to demonstrate the value of traceability in laboratory medicine to reduce between method variability in the interests of improved clinical outcomes and patient safety.

The recent publication of the two ISO standards and one technical specification listed below has a very substantial bearing on the aims of the TEP WG, which is in the process of creating educational materials aiming to explain the intentions and practical implementation of the standards in text and graphical illustrations to be published on its website www.jctlm.org.

ISO-17511:2020 In vitro diagnostic medical devices – Requirements for establishing metrological traceability of values assigned to calibrators, trueness control materials and human samples.

ISO-21151:2020 In vitro diagnostic medical devices – Requirements for international harmonization protocols establishing metrological traceability of values assigned to calibrators and human samples.

ISO/TS-20914:2019 Medical laboratories – Practical guidance for the estimation of measurement uncertainty

While paying respect to the entire substance of the standards, a primary intention is to cater for coherent understanding of the six traceability hierarchies defined in ISO-17511:2020.

A workshop on *overcoming challenges to global standardization of clinical laboratory testing: reference materials and regulations* will be held on-line on 6-10 December 2021. The primary intention of the workshop - led by Greg Miller - is to elucidate standardization from the perspectives of the regulators, manufacturers, and of Laboratory Medicine.

A group within WG-TEP led by Tony Badrick in the early phases of planning a *Workshop on EQA/PT Harmonisation* to be held – hopefully – in Paris in December 2023.

7 IFCC / ICHCLR / JCTLM 2021 Workshop on 6-10 December 2021

The Scientific Division of the International Federation for Clinical Chemistry and Laboratory (IFCC) Medicine, the International Consortium for Harmonization of Clinical Laboratory Results (ICHCLR) and the Joint Committee for Traceability in Laboratory Medicine (JCTLM) are organizing a workshop on "**Overcoming challenges to global standardization of clinical laboratory testing: reference materials and regulations**".

This Workshop, initially planned as part of the biennial JCTLM Members and Stakeholders meeting, has been reorganized and moved to a virtual mode.

The Webinar will be held during the week from 6 to 10 December 2021 with duplicate sessions per day to cover the globe, pre-recorded lectures to view in advance of each session and the meeting time will be discussion to develop recommendations.

The aim of the workshop will be to develop and publish recommendations how the laboratory medicine community can address challenges related to reference materials and regulations to more effectively achieve standardized results on a global basis.

The scientific programme is at an advanced stage of development and will be published on the JCTLM website www.jctlm.org and distributed to the recipients of this Newsletter shortly.

IFCC International Federation of Clinical Chemistry and Laboratory Medicine

International Consortium for Harmonization of Clinical Laboratory Results

JCTLM Accurate results for patient care

8 JCTLM Task Force on Reference Measurement System Implementation (TF-RMSI)

By Mauro Panteghini, JCTLM TF-RMSI Chair

JCTLM created TF-RMSI with the aim to provide guidance on traceability implementation in laboratory medicine to the IVD community. Considering major stakeholders in the field, TF-RMSI aims to:

- give to IVD *manufacturers* clarifications and proper suggestions for selecting the optimal approach for correctly implementing traceability;
- be a stimulus for *higher-order reference providers* for improving the suitability of their products, if needed;
- be a help for *laboratory professionals* in defining the analytical quality of their results.

During 2020, the TF-RMSI composition was defined with the appointment of five further members, representing major institutions actively involved in traceability implementation (for TF-RMSI membership, cf. https://www.bipm.org/en/committees/jc/jctlm/wg/jctlm-tf-rmsi). The group has started to work on a list of 13 common biochemistry measurands chosen based on: a) the number of requests received by a representative hospital laboratory; b) measurands for which CCQM comparisons were or are planned to be performed; and c) representativeness of different biological categories (e.g. electrolytes, metabolites, enzymes, etc.). The following procedural steps were adopted:

1. data extraction from the JCTLM database of available certified reference materials (CRM) and/or available reference measurement procedures (RMP) for the selected measurand;
2. description of the reference measurement system [including certified values and combined measurement uncertainty (MU)] to which each recruited CRM belongs;
3. description of the reference measurement system (including combined MU) to which each recruited RMP belongs. The available RELA information (http://www.dgkl-rfb.de:81) was used to attribute a mean experimental MU to a given clinical sample characterized as reference material by a RMP listed in the JCTLM database;
4. check of the intended use of recruited secondary (matrixed) CRM in the material's certificate and, if the intended use included "the assessment of trueness and validation of calibration of field methods used in medical laboratories", check the CRM's certificate for the information about the commutability with clinical samples for commercial procedures with which it may be potentially used as common calibrator for implementing metrological traceability;
5. check if the declared (CRM) or experimentally obtained (RMP) MU has the potential (or not) to significantly affect the MU of clinical samples, when IVD calibrator and random MUs would be added and appropriately-derived analytical performance specifications (APS) for total MU budget are applied.

As a major outcome of this study, a synopsis of higher-order matrixed RMs and RMPs listed in the JCTLM database for the selected measurands, including their main characteristics for implementing traceability and fulfilling (or not) APS for suitable MU, will be produced. The preliminary results show that traceability to the SI can be established by IVD manufacturers within the defined goal of APS for the majority of measurands. It should be however noted that, for some measurands, suitable CRMs to be used as common calibrators of IVD measuring systems are still lacking. In this case, splitting clinical samples with a laboratory performing a reference service may provide the sole practical alternative for establishing a calibration hierarchy.

Selected references

- Panteghini M, Braga F. Implementation of metrological traceability in laboratory medicine: where we are and what is missing. *Clin Chem Lab Med* 2020;58:1200-4.
- Braga F, Panteghini M. Performance specifications for measurement uncertainty of common biochemical measurands according to Milan models. *Clin Chem Lab Med* 2021 [Epub ahead of print].
- Braga F, Panteghini M. Defining permissible limits for the combined uncertainty budget in the implementation of metrological traceability. *Clin Biochem* 2018;57:7-11.

9 Future JCTLM Meetings

The JCTLM *Week*, initially planned in December 2021 at the BIPM in Paris, has been reorganized and moved to virtual mode.

- 6-10 December 2021: IFCC / ICHCLR / JCTLM Webinar on Overcoming challenges to global standardization of clinical laboratory testing: reference materials and regulations
- 13-14 December 2021: Meeting of the JCTLM Database Working Group
- 15-16 December 2021: The 23rd meeting of the JCTLM Executive Committee

10 World Metrology Day 2021: Measurement for Health

20 May is World Metrology Day, and the theme for 2021 is M**easurement for Health**.

This theme was chosen to create awareness of the important role measurement plays in health, and thus in the wellbeing of every one of us.

Further information on events can be found at www.worldmetrologyday.org and those wishing to contribute can contact the 2021 WMD Team to include links to World Metrology Day 2021 related events.

World Metrology Day is an annual celebration of the signature of the Metre Convention on 20 May 1875 by representatives of seventeen nations.

11 Metrological traceability in laboratory medicine – Report on ISO 17511-Ed2:2020

Metrological traceability in the field of laboratory medicine is defined and described in an international standard, ISO 17511, originally published in 2003 and recently revised and published as ISO 17511-Ed2:2020, *in vitro* diagnostic medical devices — Requirements for establishing metrological traceability of values assigned to calibrators, trueness control materials and human samples, 2nd Edition. At the time of publication of the first version of ISO 17511 in 2003 the concept of metrological traceability in laboratory medicine was still relatively new among many medical laboratory practitioners as well as manufacturers of *in vitro* diagnostic devices. As such, one main focus of the initial version of this international standard was on the requirements for a manufacturer of an *in vitro* diagnostic medical device to describe the calibration hierarchy for their particular device (claiming to measure a stated measurand). The calibration hierarchy is based on the availability of higher order references for the intended measurand. The new version of ISO 17511 incorporates experience gained subsequent to the implementation of ISO 17511:2003, and includes updates to the standard to ensure its alignment with other relevant standards.

Download the Special report on **Metrological traceability in laboratory medicine – Report on ISO 17511-Ed2:2020 by Hubert W. Vesper and Neil Greenberg**, April 2021, 3 pp.