

We are pleased to present the sixth issue of the Newsletter which reports on the activities of: JCTLM Working Groups and new Task Force; new entries in the database; the 2019 call for materials, methods and service nominations; and plans for 2019 JCTLM Meetings and events. We also welcome the new JCTLM Chair and new representatives to the JCTLM Executive Committee.

1 Appointment of a new JCTLM Chair

Dr Gary Myers completed his second two-year term as JCTLM Chair in December 2018. During his term, the structure and operation of the JCTLM were revised in order to open member status to new organizations and the Working Group on Traceability: Education and Promotion was established. Under his leadership the number of JCTLM member organizations increased significantly (by 50 % in number) and the awareness of the importance of traceability in laboratory medicine and its impact for accurate results for patient care has continued to grow. The JCTLM Executive Committee expressed its sincere thanks to Dr Myers for his significant contributions over the last four years.

Dr Myers is currently the Chairman of the International Consortium for Harmonization of Clinical Laboratory Results (ICHCLR), which is an organization member of JCTLM. Therefore, Dr Myers will continue to work closely with JCTLM as he was also appointed as new IFCC representative to the JCTLM Executive Committee.

During its 19th meeting in December 2018, the JCTLM Executive Committee appointed Prof. Ian Young as new Chair of the JCTLM for a renewable two-year term starting in January 2019. Prof. Ian Young is Professor of Medicine at Queen's University Belfast, and Deputy Medical Director and Consultant Chemical Pathologist at Belfast Health and Social Care Trust. In addition,

he is Chief Scientific Advisor to the Department of Health, Northern Ireland, and Director of Research for Health and Social Care. He is currently President of the Association for Clinical Biochemistry and Laboratory Medicine (UK), and a member of the IFCC SD Executive Committee. The JCTLM welcomed Prof. Young to the committee.



Handover of JCTLM Chairmanship from Dr Myers (right) to Prof. Young (left) at the BIPM in December 2018

2 New CIPM representatives to the JCTLM

At its March 2019 meeting the International Committee of Weights and Measures (CIPM) appointed two of its members as new representatives to the JCTLM Executive Committee: Dr Thomas Liew (Singapore) and Dr Sang-Ryoul Park (Republic of Korea) as Deputy.

Dr Thomas Liew is the Executive Director of the National Metrology Center of NMC, A*STAR, Singapore. Dr Sang-Ryoul Park is President of the Korea Research Institute of Standards and Science (KRISS), Republic of Korea.

Dr Park was also appointed President of the Consultative Committee for Amount of Substance: Metrology in Chemistry and Biology (CCQM) for a four-year term at the March 2019 meeting of the CIPM.



Dr Thomas Liew



Dr Sang-Ryoul Park

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

The JCTLM review process conducted in 2018 has resulted in 27 new entries in the JCTLM Database for available higher-order certified reference materials, as well as seven new published reference measurement methods, and 15 new measurement services delivered by reference laboratories. The new entries are listed below:

New entries for available Certified Reference Materials

Analyte Category	Analyte
Proteins	Amyloid Beta1-42 peptide (Aβ42) in three cerebrospinal fluid materials
	HbA1c in lyophilized human blood hemolysates at three levels
	Glycated Hemoglobin in human hemolysate buffer at three levels
Electrolytes	Calcium , Chloride , Lithium , Magnesium , Potassium and Sodium in frozen human serum at three levels

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 (<i>JCTLM Identification Number</i>)
Electrolytes	ICP-OES based reference measurement procedure for the determination of electrolytes in human blood (JCTLM C15RMP1 for Lithium, C15RMP2 for Sodium, C15RMP3 for Potassium, C15RMP4 for Magnesium and C15RMP5 for Calcium) Grote-Koska D. et al, <i>Metrologia</i> , 2018, 55 , 245-253
Metabolites and substrates	ID LC-MS/MS based reference measurement procedure for glucose in blood serum (JCTLM C14RMP11) Zhang T, et al., <i>Analytical Bioanalytical Chemistry</i> , 2016, 408 (26), 7403-7411
Nucleic acid	Digital PCR based reference measurement method for KRAS G12D/WT in solution (JCTLM C15RMP10) Whale et al., <i>Clinical Chemistry</i> , 2018, 64 (9), 1296-1307

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
Electrolytes	Lithium , Sodium , Potassium , Magnesium and Calcium in blood serum/plasma, urine, and calibration solution	Germany
	Calcium in blood serum	China
Enzymes	Alanine aminotransferase (ALT) Aspartate aminotransferase (AST) Creatine kinase (CK) Lactate dehydrogenase (LDH) Gamma-glutamyltransferase (GGT) Alpha-amylase (AMY) Alkaline phosphatase (ALP)	China
Metabolites and Substrates	Urea in blood serum	China
Proteins	HbA1c in whole blood	Japan

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

4 Call for nominations - JCTLM reference materials, methods and services

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

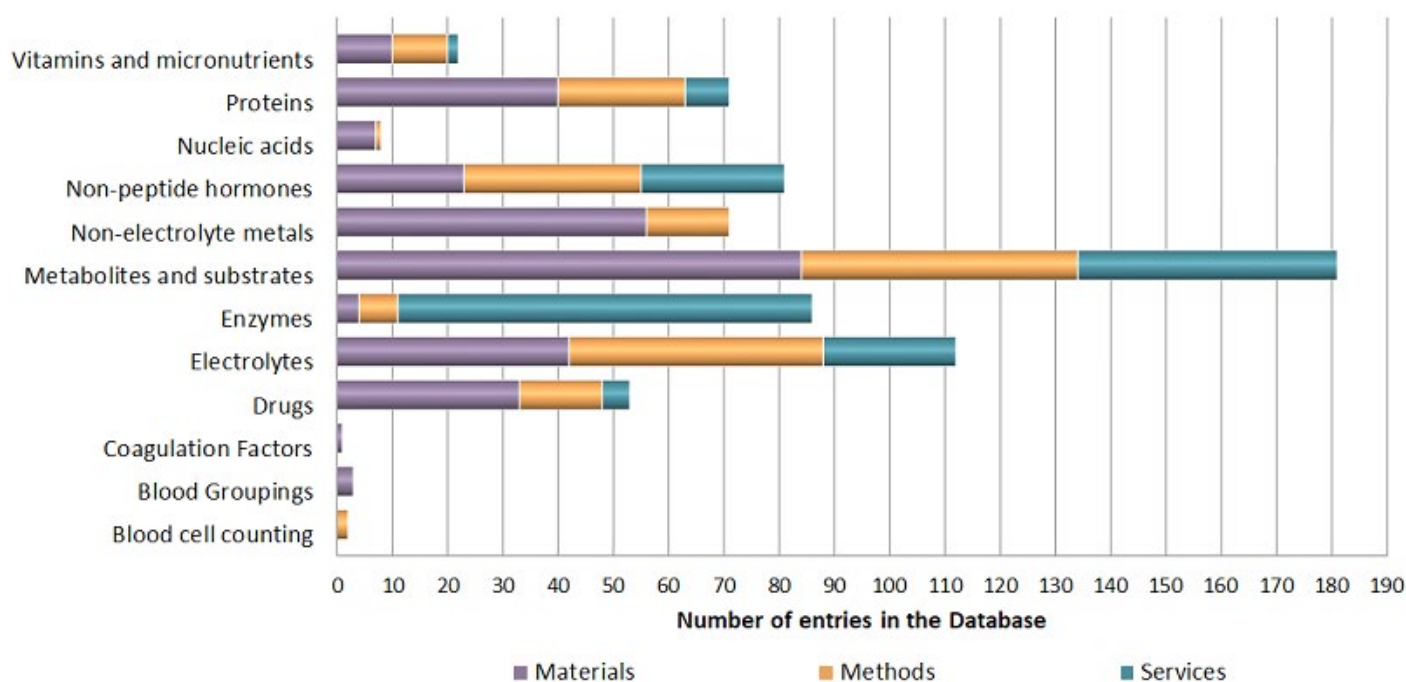
Submissions should be sent to jctlm@bipm.org no later than 31st May 2019 using the [procedures and forms available on the website](#).

5 Content of the JCTLM Database

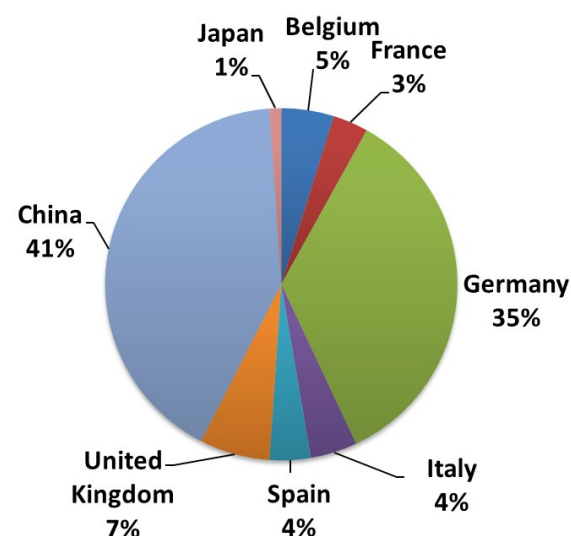
As of April 2019 the JCTLM Database contains:

- 303 entries for certified reference materials that cover about 170 different analytes and represent 200 measurands in 11 categories of analyte ;
- 201 reference measurement methods that cover about 90 different analytes and represent 160 measurands in 10 categories of analyte;
- 187 reference measurement services delivered by 19 reference laboratories and two national metrology institutes in eight countries and which cover 40 different analytes and represent 103 measurands in seven categories of analyte. The pie chart below shows the distribution of the services listed by region of origin of the service provider.

JCTLM Database entries as of April 2019



Geographic distribution of reference measurement service providers as of April 2019



	Materials			Methods			Services		
	DB Entries	Analyte	Measurand	DB Entries	Analyte	Measurand	DB Entries	Analyte	Measurand
Blood cell counting	-	-	-	2	1	1	-	-	-
Blood groupings	3	3	3	-	-	-	-	-	-
Coagulation factors	1	1	1	-	-	-	-	-	-
Drugs	33	24	27	15	11	18	5	3	9
Electrolytes	42	6	12	46	7	28	24	6	22
Enzymes	4	4	4	7	7	14	75	7	28
Metabolites and substrates	84	52	57	50	15	32	47	10	35
Non-electrolyte metals	56	31	38	15	7	15	-	-	-
Non-peptide hormones	23	11	16	32	14	20	26	10	32
Nucleic acids	7	2	2	1	1	1	-	-	-
Proteins	40	29	33	23	19	21	8	2	7
Vitamins and micronutrients	10	10	10	10	6	6	2	2	2
Total	303	173	203	201	87	156	187	40	135

Measurand corresponds to an Analyte/ Matrix combination

6 A new JCTLM Task Force focusing on the implementation of reference measurement systems

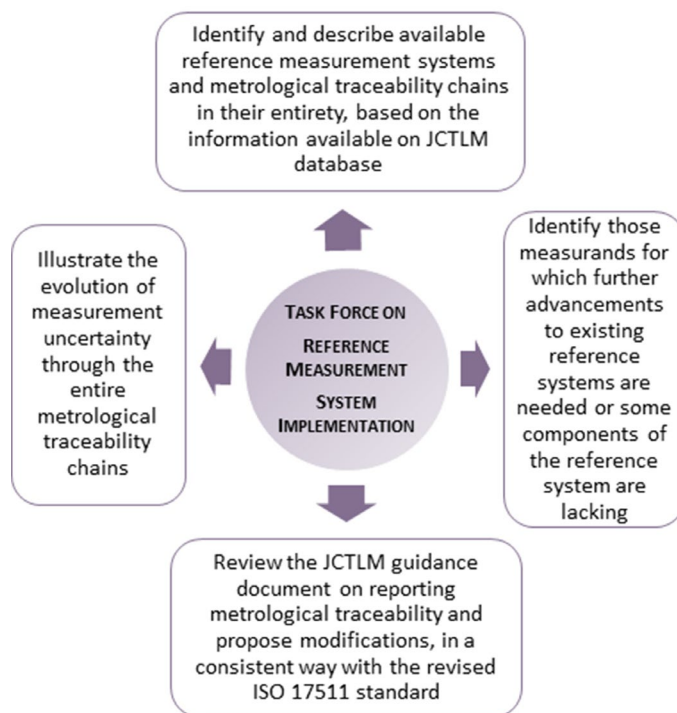
Mauro Panteghini¹, Federica Braga¹, Robert Wielgosz²

¹ Research Centre for Metrological Traceability in Laboratory Medicine (CIRME), University of Milan, Milano, Italy.

² Bureau International des Poids et Mesures Pavillon de Breteuil, Sevres Cedex, France.

Only a brief description of metrological traceability and associated uncertainty is often provided with commercial calibrators. The information is often limited to the name of higher-order reference materials and/or reference procedures to which the assay calibration is traceable, without any description of implementation steps. Information such as the applied calibration hierarchy, the measurement uncertainty associated with calibrator, and the employed acceptable uncertainty limits is often partly reported. To fully verify the characteristics of commercial measuring systems, laboratory users should be able to access the following: a) an indication of higher-order references (materials and/or procedures) used to assign traceable values to calibrators, b) which internal calibration hierarchy has been applied by the manufacturer and a detailed description of each step, and c) the combined measurement uncertainty value of commercial calibrators, and which, if any, acceptable limits for uncertainty of calibrators were applied in the validation of the measuring system.

Accumulated experience is showing that standardization projects not only have to address metrological traceability but should also consider the efficacy of its implementation. Previous analyses highlighted how strongly the measurement uncertainty may be dependent on the type of traceability chain adopted by the IVD manufacturers to implement the traceability of their calibrators. It has been shown that the selection of different types of traceability chains (all employing reference materials and procedures listed in the JCTLM database) may lead to different combined uncertainties at the level of commercial calibrators, not always permitting to fulfil the suitable uncertainty budget at the level of clinical sample measurements. Therefore, in order to aid IVD manufacturers in the implementation of metrological traceability, the identification and definition of available reference measurement systems and of metrological traceability chains in their entirety and not just in their main components (i.e., reference materials and methods) can be extremely helpful. With this in mind, the JCTLM Executive Committee approved, during its last annual meeting, the creation of the **JCTLM Task Force on Reference Measurement System Implementation (TF-RMSI)**, with the aim to provide guidance on reference measurement system implementation to the IVD community. This activity will be timely with the upcoming publication of the revised ISO 17511 standard that lays out the requirements for establishing reference measurement systems and their implementation by IVD manufacturers.



The figure shows the terms of reference for TF-RMSI. A key output will be the identification of available reference measurement systems and metrological traceability chains in their entirety. The illustration of the evolution of measurement uncertainty through the entire metrological traceability chains and the identification of measurands for which further advancements to existing reference systems are needed or some components of the reference system are lacking will allow to indicate areas for improvement for reference providers and IVD manufacturers and to help prioritise future efforts. Based on the work of the TF-RMSI and the content of the revised ISO 17511 standard, the JCTLM guidance document on reporting metrological traceability will be reviewed. The progress of the TF-RMSI activity will be reported at future meetings of JCTLM members and stakeholders, where next steps on promotion of this work and future collaborative efforts between JCTLM and appropriate organizations will be proposed.

Selected references

- Braga F, Panteghini M. Verification of in vitro medical diagnostics (IVD) metrological traceability: responsibilities and strategies. *Clin Chim Acta* 2014;432:55-61.
- Braga F, Infusino I, Panteghini M. Performance criteria for combined uncertainty budget in the implementation of metrological traceability. *Clin Chem Lab Med* 2015;53:905-912.
- Braga F, Panteghini M. Defining permissible limits for the combined uncertainty budget in the implementation of metrological traceability. *Clin Biochem* 2018;57:7-11.

7 Importance of metrological traceability for EQA

External Quality Assurance is mandatory for many laboratories and when used effectively it can provide many opportunities for improvement including the following:

- Characterize test bias and imprecision across multiple methods
- Identify interfering substances and quantify their effects across multiple methods
- Provide clinical laboratories with reliable information for replacing unsatisfactory methods
- Identify clinical laboratories that are at risk of poor performance
- Satisfy accreditation and regulatory requirements
- Assessment of method robustness to clinically relevant interference
- Assessment of individual laboratory performance
- Audit of wider aspects of analytical performance and educational activities.

However, because EQA schemes have access to large volumes of method specific data which can be used at a more global level they can assist in the harmonization of methods. This data can be used as a post market surveillance process.



Dr Tony Badrick

However, EQA schemes are often tailored to and operate at a local level rather than globally and this limits their ability to perform this key role. In this Newsletter's Special Report, Dr Tony Badrick shares his views on how EQA schemes can work together and provide much needed information on an aspect of traceability in laboratory medicine.

Download the [Special report on The role of EQA in monitoring traceability by T. Badrick, April 2019, 3pp.](#)

8 Activities of the WG-TEP

After a hectic year of activity in 2017 the Working Group for Traceability, Education and Promotion (WG-TEP) settled to a year of steady progress in 2018. Achievements included:

Website:

The website www.jctlm.org continues to be updated on a regular basis with news items and additional freely available resources. The website is well used with an excellent global profile and feedback is positive. Revision of the home page took place in March 2019.

Webinars:

WG-TEP completed its task of publishing ten short webinars on the IFCC eAcademy. The webinars can be accessed directly [here](#).

Presentations at conferences:

During 2018, presentations on traceability in laboratory medicine were made in nine countries. The JCTLM was invited to present to the 26th meeting of the General Conference on Weights and Measures (CGPM) held in Versailles, France in November 2018. The presentation is available [here](#).

Auspices:

JCTLM Auspices were awarded to scientific meetings in five countries. To apply for JCTLM auspices, access the form [here](#).

Publications:

Google scholar reveals >350 publications mentioning traceability and laboratory medicine in 2018, almost 100 of these mentioned JCTLM. Key publications are listed in the Publications section of www.jctlm.org. To list other key publications contact the Secretariat at jctlm@bipm.org.

Newsletter:

The last annual Newsletter was published in April together with a special report on commutability by Neil Greenberg and Greg Miller.

Survey of JCTLM Members:

A survey of JCTLM Members was conducted to assess the level of satisfaction with JCTLM services. Overall, the responses indicated that Members gave 'very valuable' or 'valuable' ratings to the JCTLM database; the resources on www.jctlm.org; and the JCTLM channels of communication.

Future work

The WG-TEP has two active projects for 2019:

- Agreeing and future workstreams. These will be notified to JCTLM Members shortly
- Organizing the JCTLM scientific Meeting entitled 'Accurate results for patient care'. A separate item on this meeting appears in this Newsletter.

9 Recent article on IVD Regulation published

The European Union *In Vitro* Diagnostic Medical Device Regulation 2017/746 (IVDR) was published on 5 May 2017 as a replacement for the *In Vitro* Diagnostic Directive 98/79/EC (IVDD). The Regulation is the most direct form of EU law and is immediately applicable and enforceable in all Member States. Since IVDs operate in a global market it is reasonable to expect that the IVDR will impact IVDs at a global level. A five-year implementation period applies to the IVDR.

Adoption of the IVDR has several implications for the diagnostics industry that manufactures and distributes IVDs. There are also implications for the laboratory medicine specialists who use IVDs.

From a JCTLM perspective the IVDR contains a clear statement that ‘the metrological traceability of values assigned to calibrators and/or control materials shall be assured through suitable reference measurement procedures and/or suitable reference materials of a higher metrological order’.

An article that summarizes the IVDR and its implications was recently published in the IFCC e-News (pages 21-24). Gary Myers, former Chair of JCTLM, is the lead author. The article is available from: <http://www.ifcc.org/media/477657/ifccenewsfebruary2019.pdf>

10 Accurate Results for Patient Care Meeting 2019

The biennial JCTLM scientific meeting will be held on Monday and Tuesday 2-3 December 2019 at the BIPM in Sèvres near Paris. All JCTLM Members are invited to attend and to contribute to the scientific programme. The meeting is open to anyone interested in initiatives to reduce between-method variability in laboratory medicine.

The scientific programme is at an advanced stage of development and will be published in full in May, when registration will open. However, there is still the opportunity for JCTLM Members to influence the content of the final programme. Sessions at the meeting will include:

- Challenging the status quo
- New approaches to improving quality in laboratory medicine

- International standards and regulation of IVDs
- Commutability
- Harmonization of methods for difficult analytes
- International projects to achieve standardization/harmonization

Poster presentations are also invited, with discussion taking place in a relaxed and supportive environment.

The registration fee for the meeting is €75 to cover catering costs and administration. An optional dinner will be held during the evening of 2 December for which an additional fee will apply.

Suggestions for programme content should be sent to Secretariat at jctlm@bipm.org

11 Seeking new experts members for JCTLM review teams

The review teams of the JCTLM provide the technical expertise necessary to review nominations for certified reference materials, reference measurement methods and services.

Nucleic acid, Proteins, Metabolites and substrates and Vitamins. To apply for review team membership please contact the Secretariat (jctlm@bipm.org).

The JCTLM is looking for new members for contributing to its review teams with an expertise in the field of Enzymes,

The application form and procedures are available [here](#).

12 Future meetings

Meetings held under the auspices of the JCTLM

- 20-27 June 2019: ReMiND 2019 - Biomolecules in Neurodegenerative Diseases, PTB, Braunschweig (Germany). See [Conference website](#)
- 28 November 2019: 13th International Scientific Meeting of the Centre of Metrological Traceability in Laboratory Medicine (CIRME) “The internal quality control in the traceability era”, CIRME, Milan (Italy). See [Meeting programme](#)

Future JCTLM meetings

- 2-3 December 2019: JCTLM Members’ and Stakeholders’ Meeting, BIPM, Sèvres ; [Workshop Website](#)
- 4 December 2019: JCTLM TEP WG meeting, BIPM, Sèvres
- 4 December 2019: JCTLM Database Working Group meeting, BIPM, Sèvres
- 5-6 December 2019: Meeting of the JCTLM Executive Committee, BIPM, Sèvres