

**Report of the 21st meeting of the JCTLM Executive Committee  
5-6 December 2019, BIPM, Sèvres, France**

**List of participants:**

Dr G. Myers (JCTLM Acting Chairman, IFCC)  
Dr G. Beastall (IFCC, JCTLM WG-TEP Chair)  
Dr R. Wielgosz (JCTLM Executive Secretary, BIPM)  
Dr S. Maniguet (JCTLM Secretariat, BIPM)  
Dr T. Liew (CIPM)  
Dr G. Jones (ILAC)  
Ms M. Bednarova (ILAC)  
Dr Q. Liu (JCTLM DB WG vice-Chair, AG1)  
Prof. M. Panteghini (JCTLM DB WG vice-chair, AG2)  
Dr K. Phinney (JCTLM DB WG vice-Chair, AG3)  
Mr T. Fawcett (ICSH)

Apologies received:

Dr M. Milton (BIPM)  
Dr A. Kessler (IFCC)  
Prof I. Young (JCTLM Chairman, IFCC)  
Dr Sang-Ryoul Park (CIPM)

Dr Myers opened the meeting and welcomed the participants.

**1. Approval of the agenda [JCTLM-EXEC/19-01]**

Dr Myers said that a discussion point on the outcomes of the JCTLM Mini Workshop on “Working together towards Standardization in Laboratory Medicine – co-ordination of international activities” held on 4 December was needed and Dr Jones asked for an additional discussion point on JCTLM instructions for industry use. The changes to the agenda were approved and new discussion items would be discussed under agenda points 10 and 17, respectively.

**2. Report of 19<sup>th</sup> JCTLM Executive Committee Meeting [JCTLM-EXEC/19-02]**

There were no comments on the report of the 20<sup>th</sup> Executive Committee meeting, which had been finalized in March 2019 and published on the [BIPM JCTLM website](#).

**2.1 Review of action points arising from the 20<sup>th</sup> meeting [JCTLM-EXEC/19-02a]**

Dr Wielgosz summarized the action items from the previous meetings that were still in progress:

**Action (A/17-29): RW to contact Dr M. Nübling (PEI) to discuss the possibility to work jointly/closely with WHO in drafting a discussion paper for December JCTLM M&S meeting; GB to draft a bullet point paper prior developing a full discussion paper.**

Dr Wielgosz said that WHO’s contact had recently changed. This action would be followed up on after the meeting in collaboration with the representatives from NIBSC who attended the JCTLM Workshop and offered to help to engage in further discussions on metrological traceability /standardization /harmonization with the WHO.

**Action (A/18-02): IY/RW will follow up on this action after the meeting and propose a strategy for developing an induction process for new EC members.**

This action was completed and would be reported under agenda point 4.1.

**A/18-03: This action was taken over by the revision of the DoC after consultation with BIPM legal advisor which was being circulated for comments to ILAC, IFCC and CIPM until end of June.**

This action was completed and would be reported under agenda point 3.

**A/18-14: IY/RW will follow up on this action after the meeting and propose a strategy for developing a process to avoid conflict of interest during the JCTLM review process.**

This action was ongoing and progress would be discussed under agenda point 6.2.

**A/18-15: Secretariat will launch a survey among the review team members to look at what ISO standards they have access to by end of June**

BIPM conducted an evaluation survey among the members of the review teams to test what ISO Standards used in JCTLM process they have access to, and the response rate was only 30%. It showed that 70 to 80% of those who responded have access to the main ISO standards that laid down JCTLM review requirements with less than 50% of the respondents having access to other standards that are normative in the main ones.

The Committee noted the low rate of responses from teams' members and supported the recommendation from the Database WG to re-review the review teams' membership for the next 5 years. It further requested that teams' members should be asked to confirm that they have access to the ISO Standards that are the basis for the JCTLM Review.

In line with the recommendation of the DBWG, the Committee also agreed that JCTLM should continue to engage in producing resources for training new review team members. It further requested that adequate self-training support on ISO standards and JCTLM acceptance/review criteria for new members joining the review teams and for laboratory staff submitting nominations for the first time should be developed. Dr Wielgosz commented that such a project would require the allocation of adequate technical and financial resources.

The Committee recognized the need to define the scope for a project on training for JCTLM contributors.

**A/18-17: Secretariat will follow up on this action after the meeting and send reminder to the two laboratories identified with no results in the RELA Scheme for 2015-2017.**

The Secretariat contacted the service providers not fulfilling one of the JCTLM requirements for regular participation in EQAS Scheme to confirm with them their service status and inform them they would need to participate in an EQAS in order to address the non-compliance. The response from one of the questioned laboratories was being reviewed by the RELA advisor in order to confirm that the evidence provided was suitable to fulfill JCTLM criteria.

**A/18-16: QL will lead the review the text of the document procedure DB WG P-04a and circulate a draft of a revised procedure for comments from sub-group by end of June.**

This action was ongoing and progress would be discussed under agenda point 6.4

**A/18-18: IY/AK will follow up on this action and draft proposal for revision of JCTLM rules for regular participation in EQAS Scheme.**

This action was ongoing and progress would be discussed under agenda point 6.3

### **New Actions:**

**Action(A/19-01):** Secretariat to contact members of review teams regarding completion/or reappointment of their 5 year terms as review team members, and access to the ISO Standards.

**Action(A/19-02):** Dr Wielgosz to develop a plan and scope for a training project on ISO Standards.

**Action(A/19-03):** RELA advisor to confirm the adequacy of the evidence provided by the service laboratory to fulfill JCTLM criteria in relation to its participation in the EQAS Scheme for 2015-2017.

### **3. Progress with revision of JCTLM Declaration of Cooperation**

Dr Wielgosz reported that the final version of the revised text of the Declaration of Cooperation (DoC) and its Appendices had been circulated for signature to the three parties, the ILAC, IFCC and CIPM, and the document has been structured to allow other organizations to join the JCTLM Executive Committee by procedures established by the JCTLM Executive Committee. This would avoid the Declaration document having to be signed for each new member in the future. Additional procedures for accession to and exclusion from the JCTLM EC would be established in the next year.

#### **3.1 ICSH Membership for JCTLM Executive Member Status**

Following the signature of the DoC by the three parties and the recommendation from the JCTLM Executive Committee at its last annual meeting to accept ICSH membership of the Committee, the Committee approved the ICSH as new Executive Committee Member during the meeting.

**Action (A/19-04):** IY/RW to draft an additional procedure for accession and termination of JCTLM Executive Member Status which is referred to in the DoC for discussion at the Executive Meeting in December 2020.

### **4. JCTLM membership**

#### **4.1 Developing an induction process for new EC members**

Dr Wielgosz informed the Committee of the proposed several options for the induction process for new Executive Members including providing new members with relevant JCTLM documentation, organizing a teleconference to introduce websites and procedures, as well as a face-to-face meeting at the BIPM with presentations on processes and procedures by JCTLM Secretariat. The Committee agreed with the proposed approach that would be trialed with the ICSH at the beginning of 2020, and later formalized in a written procedure document.

**Action (A/19-05):** BIPM to draft a procedure for an induction process for new EC members of JCTLM Executive Member Status for discussion at the Executive Meeting in December 2020.

#### **4.2 Members' biennial activity reports [JCTLM-EXEC/19-03]**

Dr Myers reported that about half of the JCTLM member organizations have already sent their biennial activity reports for the period 2018-2019 for consideration by the Executive Committee, and all of these were included in the document JCTLM-EXEC19-03. The Committee acknowledged the quality of the reports provided and also agreed to review and address the issues and questions submitted in these reports.

It further requested that the document for the activity reports should be made available on the public website.

**Action (A/19-06):** Secretariat to post JCTLM Member organizations' activity reports on the BIPM JCTLM Members dedicated webpage

## **5. JCTLM Governance**

### **5.1 Representation on the Executive**

Following the approval of the ICSH as a new Executive Committee Organisation Member, the ICSH confirmed the nomination of Mr. Terry Fawcett and Dr. Paul Harrison as representatives of the ICSH at the Executive Committee meeting. The Committee welcomed these nominations.

### **5.2 JCTLM WG Chairs**

Dr Beastall informed the Committee that he submitted to the Chairman of the JCTLM in advance of the meeting a list of nominees who could be contacted to succeed him as Chair of the TEP WG, and the appointment of the new Chairman of the TEP WG would be made by email after the meeting. He also confirmed the Committee that IFCC Office agreed to continue to maintain jctlm.org website with the assistance of Paola Bramati.

### **5.3 Funding of the JCTLM Secretariat**

As reported at the previous meeting the running cost for 2020 would be similar as for 2019, with some additional costs related to the running of the Stakeholder meeting. It was agreed that BIPM and IFCC would again share the JCTLM Secretariat costs on a 50:50 basis for 2020.

### **5.4 JCTLM Database**

Dr Maniguet presented the status of the database as of December 2019.

In February 2019, 27 entries for certified reference materials, seven reference measurement methods, and 15 reference measurement services were published in the JCTLM Database following the approval by the Executive of nominations reviewed during DB WG cycle 15 for materials and methods and cycle 13 for services. In addition, 21 entries covering six certified reference materials were delisted from the JCTLM Database and placed in the PDF file for no longer available materials. The Secretariat informed the Committee that an additional set of 50 entries of CRMs would be removed at the beginning of 2020 after the producer confirmed the availability of his CRMs listed in the JCTLM Database. The Committee commented on the need to raise awareness with the material producer of the importance of a submission for the renewed batch of CRM.

The current status of the database as of December 2019 was as follows:

- 295 certified reference materials (CRMs) from 14 producers including 12 NMIs/DIs,
- 201 reference measurement methods covering about 100 measurands, and
- 187 reference measurement services covering 45 analytes. These services were delivered by 18 reference laboratories accredited for compliance against ISO 15195 and IEC/ISO 17025 as Calibration laboratories, and by two National Metrology Institutes (NMIs).

In response to the request from the EC at its last meeting for improving the search facility on reference measurement systems, the Secretariat consulted the external company in charge of the routine maintenance activity and reported on technical issues that would need to be taken into account for future functional improvements. There has been no major changes on functionalities since 2010. The first version of the application was implemented in 2006 for listing the materials and methods, the second version was released in 2007 for listing the services, and finally the application was extended to implement ISO 15194:2009 requirements for materials in 2010. The current version of application had shown itself to be robust over the years, but its web interface was not designed for new generation supports, e.g. tablets & mobiles, and did not include a free search text engine. In addition, the fact that the application was based on an old Java Framework would involve extra costs for future improvements and changes on the web platform without changing the Framework. The global estimate from the external company for updating the application to allow for improvements of the search facility confirmed this assumption.

In the discussion that followed the Committee agreed that the obsolescence of the application should be anticipated and requested that technical specifications taking into account an update of the application and inclusion of new generation functionalities should be drafted in the view of launching a call for tender in 2020. At the same time funding for a new database would need to be found from external sources.

**Action (A/19-07):** JCTLM Secretariat to draft technical specifications for updating the JCTLM Database web system and application and launch a call for tender.

## **6. Revision of JCTLM quality manuals**

### **6.1 Procedure for accession and termination of JCTLM Executive Member Status which is referred to in the DoC**

This agenda item was discussed under agenda point 3 and the necessary procedures for accession to and exclusion from the JCTLM EC would be established in the next year.

### **6.2 Process to avoid conflict of interest during the JCTLM review process**

Dr Wielgosz informed the Committee of the proposal to modify the necessary existing procedures to include a clause to avoid the conflict of interest during the JCTLM review process. Amendment to the procedure foresaw a sentence to indicate that any team member being also representative of the nominating organization would be excluded from the review. The Committee agreed with the proposal and also requested to allow for a clause of confidentiality until the review ends which would be applied when a member of the review team was affiliated with the nominating organization.

**Action (A/19-08):** Secretariat to modify the relevant procedure documents to include a clause on conflict of interest and confidentiality which would be applied during the review process.

### **6.3 Revision of JCTLM rules for regular participation in EQAS Scheme**

Dr Wielgosz said that following the decision taken by the EC at its last meeting, JCTLM rules for regular participation in EQAS Scheme were under review and there would be no change for next review cycle. The view from the review group was that there was a need to harmonize JCTLM rules with the accreditation requirements applied at the international level,

and JCTLM was in a position to provide advice on what it considered to be sufficient frequency, based on its knowledge of potential risks resulting from modifying the frequency.

The Committee noted that an input from ILAC representative would be beneficial to anticipate harmonization of the frequency of participation, which applies differently among national accreditation bodies (NAB), and also join the Quality Review Team to review other JCTLM quality procedures.

**Action (A/19-09):** SM/MB to review JCTLM quality procedures including JCTLM rules for regular participation in EQAS Scheme

#### **6.4 Revision of the document procedure DB WG P-04a [JCTLM-EXEC/19-04]**

Dr Liu presented a model for demonstrating equivalence of nominated materials with materials already listed in the database during the meeting of the DBWG. As a result of the discussion, the WG recommended that a small group should revise the proposed model in order to anticipate the level of comparability which would be required with respect to type of analyte (well defined/complex), number of materials used in a comparison study and how equivalence demonstrated via the system of the CIPM MRA for NMIs could be incorporated.

**Action (A/19-10):** SM/RW/QL/MQ/KP to revise the procedure document P04-A to propose a model taking into account the comparisons performed within the framework of CIPM MRA, the type of analyte for which the well-established CCQM system could be employed to demonstrate equivalence, and also the number of materials that would be required for a comparability study.

#### **6.5 Evolution of nominations being received and impact on JCTLM quality process**

The Committee discussed the rejection rate of the nominations that were submitted for review by JCTLM and noted it has been stable over the last two-three years review cycles. Some members of the Committee commented that raising awareness on conducting commutability campaign was one of the key issues that JCTLM needed to address in order to increase the level of acceptance at the first review cycle. The Committee agreed that a Workshop should be organized to reach CRM producers and IVD industry in performing those campaigns.

**Action (A/19-11):** JCTLM Chair to draft a proposal for JCTLM Workshop on Commutability at EuroMedlab Meeting in 2021 in Munich.

#### **6.6 Discussion on possibility of inclusion of ISO 21151 compliant harmonization protocols in the JCTLM DB**

Dr Myers said that the publication of the new standard ISO 21151 on Requirements for establishing metrological traceability of values assigned to calibrators, trueness control materials and human samples, was expected in 2020, and this in parallel with the publication of the reviewed ISO17511. He further opened the discussion on the possibility to include ISO 21151 compliant harmonization protocols in the JCTLM Database.

The Committee recognized the importance of the new standard, which included harmonization protocol as one approach to achieve metrological traceability, and requested clarification about whether the standard would be published as harmonized standard for the EU IVDR, and what information would be published in the JCTLM Database, considering that it would result in updating the database application. It mentioned the necessity to explore a case study in close collaboration with the International Consortium for Harmonization of Clinical Laboratory Results (ICHCLR), and ICSH.

**Action (A/19-12):** JCTLM EC members to review new standard ISO 21151 to highlight what information would be suitable for publication in the JCTLM Database, for discussion during a conference call.

## **7. Report from the JCTLM WG on Traceability Education and Promotion [JCTLM-EXEC/19-12]**

Dr Beastall presented the document JCTLM EXEC/19-12 which included the annual report of the TEP WG for the JCTLM Executive Committee. He said that the website continued to be updated on a regular basis with news items, webinars, publications and presentations at conferences, and the website homepage has been updated as planned.

Dr Beastall further reported that the TEP WG held a meeting on 4 December 2019 at the BIPM and highlighted the main recommendations from the meeting discussions.

The TEP WG took the lead role in the organisation of the JCTLM Workshop held on 2/3 December which included a parallel session for the first time. The capacity audience and increased number of posters indicated support for the Workshop. The WG recommended it should be held again in December 2021 and also questioned the BIPM as a suitable venue. Dr Beastall would ask the WG-TEP to investigate the cost and the options for hosting the next Workshop to larger capacity venue.

The TEP WG discussed updating membership to move the WG membership to be reasonably representative of the wider JCTLM membership (geographically and professional roles). Dr Beastall informed the Committee that most of the members have already confirmed their participation and other WG members would be invited to indicate whether they wish to continue or to stand down at the end of 2019. The TEP WG re-elected Dr Maniguet as Secretary and recommended four new persons who expressed interest in joining the TEP and invited an ICSH representative to participate to the group.

The TEP WG allocated individuals to progress the agreed future workstreams for completion at the end of 2020 and other members would be invited to indicate what work items they wish to contribute to.

The Committee approved the recommendations from the TEP WG and requested that the cost and options for hosting the Workshop outside the BIPM should be looked at. It further invited EC members from Asia Pacific region to propose additional experts for the TEP WG.

**Action (A/19-13):** Secretariat to investigate the cost and the options for hosting the next Workshop to larger capacity venue outside the BIPM.

## **8. Report from the Task Force Group of Reference Measurement System Implementation**

Prof. Panteghini informed the Committee that the two members of the TF- RMSI drafted a manuscript on the review status on implementation of metrological traceability in laboratory medicine, using creatinine as a case study, and looking at the higher-order materials, methods and services provider available in the JCTLM Database. This has been circulated for comment to the EC in 2019 and was about to be published in Clin. Chem. Lab. Med. Journal.

He recalled that this opinion paper aimed at providing guidance to IVD manufacturers for implementing traceability to higher-order references and to end-users in terms of MU of different options (calibration chains established) for their clinical use. The Committee commented that this raised a key issue of how achievable MU should be compared to calculated analytical performance specifications for measurements in the medical laboratory. The Committee agreed that the study should be extended to a short list of measurands covered within the JCTLM Database and for which there had been CCQM comparisons as well as considering their clinical impact.

The Executive recommended also to expand the membership of the Task Group (wider professional and geographical coverage), and to recruit additional members by contacting JCTLM Member organisations.

**Action (A/19-14):** Prof Panteghini to recruit further members for the TF-RMSI to carry out an additional study.

## **9. JCTLM DB WG: Approval of Recommendations**

Dr Maniguet presented the summary of the nominations for reference materials, reference measurement methods and reference measurement services with the final DB WG's recommendations that had been submitted for review as part of cycle 16 for materials and methods and cycle 14 for services.

There were 153 new nominations and 42 outstanding nominations from the previous year that had been distributed for consideration to nine JCTLM review teams in 2019.

There were 98 nominations for reference materials for five groups of analytes, 134 nominations for reference measurement methods for five groups of analytes which had been submitted for CRM/RMP review cycle 16, as well as 29 nominations for services for five groups of analytes which had been submitted for RMS review cycle 14.

Dr Myers said that the Database WG met on 4/5 December and successfully completed the review of all review teams' recommendations concerning these 195 nominations. All of these are summarized in the following sub-sections for each group of analytes including final Database WG recommendations.

### **9.1 IFCC CDT method and Drugs material appeals**

Dr Wielgosz said that the IFCC WG on CDT appealed the 2018 JCTLM decision for not listing their method and the DB WG requested that the review team should provide a complete dossier of the review of the method nomination and team's recommendation with regard to the appeal for consideration to the JCTLM Executive Committee.

**Action (A/19-15):** Secretariat to contact Proteins review team to provide a complete dossier with information concerning the reviews of the CDT Method and their decision to maintain their recommendation for requesting corrective action for consideration by the EC.

The producer of a sirolimus material in blood challenged the 2018 JCTLM recommendation to revise the intended use statement in the certificate of the material in order to waive the non-compliance for inclusion in the database. The review team would provide a complete dossier on the review of the material nomination and team's recommendation in regard to the appeal decision for consideration by the JCTLM Executive Committee.

**Action (A/19-16):** Secretariat to contact the Drugs review team to provide a complete dossier with information on the review of the Sirolimus material in blood and the

recommendation from the review team in regard to the producer's response appealing the EC recommendation, for consideration by the EC.

## **9.2 Approval of Cycle 16 RM and RMP and Cycle 14 RMS**

### **9.2.1 Blood cell counting and typing**

Dr Wielgosz reminded the Committee that there was an outstanding nomination submitted by the ICSH for a platelet counting reference measurement method for which the final recommendation had been deferred to the EC decision after last year's review of the Blood cell counting team's recommendation.

The view of Executive was that there were key issues that needed to be resolved prior resubmission to JCTLM. Major concerns were about a comparison study with the listed PTB method and corrective action for uncertainty calculation for GUM compliance. Those were discussed with the ICSH which expressed willingness to address the issues. The Committee agreed that the recommendation would then be formalised in the report for distribution to ICSH.

**Action (A/19-17):** EC to amend the review report of the ICSH outstanding method in accordance with the EC recommendation.

There was a new nomination for a reference measurement method submitted for the determination of erythrocyte concentration in blood for which the final recommendation was not yet ready for discussion at the DBWG meeting. The review of this nomination was pending resolution of the review of the previous Platelet count method nomination, which was outstanding from 2018 review cycle.

In the discussion that followed the Committee agreed to provide support to the review team to resolve the reviews of the Blood Cell Counting. It also requested a review and update of the team membership in collaboration with the team leader.

**Action (A/19-18):** EC to liaise with Blood cell counting team in order to review the team membership and to resolve the review of the erythrocyte method.

### **9.2.2 Drugs [JCTLM-EXEC/19-11]**

There were 12 nominations for certified reference materials and four nominations for reference measurement methods for immuno-suppressive drugs that was carried out by the review team for Drugs and of these 12 nominations for CRMs were being recommended for listing in the JCTLM Database.

There were 12 nominations for pure drugs of abuse certified reference materials for which the producer submitted data/information and revised certificate to respond to non-compliances observed during last year review cycle. The DBWG recommended the listing of the materials considering that corrective actions were satisfactory.

There were also nominations for an isotope dilution LC-MS/MS based candidate reference method for the quantification of cyclosporine A, tacrolimus, sirolimus and everolimus in human whole blood for which the recommendation for listing in the database was pending the resolution of non-compliances. Major concerns were about the lack of method publication in a journal and the calculation of the method uncertainty, and comparison study data for compliance with JCTLM-P04b procedure.

The Committee approved the DB WG's recommendation for the Drugs materials.

### **9.2.3 Electrolytes [JCTLM-EXEC/19-05]**

There were four nominations for reference measurement services that were reviewed by the review team for Electrolytes, and none were being recommended for inclusion in the JCTLM Database.

The Committee approved the DB WG's recommendation for Electrolytes nominations.

### **9.2.4 Enzymes [JCTLM-EXEC/19-06]**

There was a nomination for an ALP certified value of the multi-enzyme CRM and a nomination for a reference measurement service that were performed by the JCTLM review team for Enzymes. Of these, the nomination for an alkaline phosphatase in blood serum/plasma from a Chinese calibration laboratory was being accepted for listing in the JCTLM Database.

The Committee approved the DB WG's recommendation for Enzymes nominations.

### **9.2.5 Metabolites and Substrates [JCTLM-EXEC/19-07]**

There were 105 nominations related to certified reference materials, two nominations for reference measurement methods and ten nominations for reference measurement services that were reviewed by the review team for Metabolites and Substrates, and of these five reference measurement services were being recommended for inclusion in the JCTLM Database.

## **Materials**

There were nine nominations for certified reference materials for serum Creatinine, serum Cholesterol, and Amino Acids in human plasma, and all of these were not being recommended for inclusion in the JCTLM database until the producer addresses the non-compliances. Issues for all materials concerned the lack of hierarchical position statement both on the certificate and on the certification report, as well as the lack of long-term stability data and specification of number of runs/replicates used for value assignment and measurement uncertainty. In addition, commutability study data for cholesterol and AA would need to be provided to support the intended use statement in the certificate.

The DBWG noted the observation that the equivalence evaluation for Cholesterol and AA materials did not include all the materials already listed, and recommended that a successful participation of the producer in CCQM Study should also be taken into account and considered as suitable additional evidence for demonstrating the extent-of-equivalence of nominated materials with already listed CRMs.

The remaining submissions were 96 nominations covering two multicomponent materials for 37 amino acids certified in plasma and 59 organic acids certified in urine, and all of these were not being accepted for inclusion in the JCTLM Database. Critical non-compliance concerned the characterization of the materials. The DB WG decided to postpone the recommendation for these nominations until after a DBWG re-review of the initial review observations.

## **Methods**

There was a first nomination for an ID LC-MS/MS reference measurement procedure for total Glycerides and a second nomination for an ID LC-MS reference measurement procedure for urea in serum, for which the recommendation for JCTLM listing was pending the resolution of observed non-compliances. Major concerns were about the lack of interference study and limit of detection.

## **Services**

The DBWG recommended the listing in the database of four nominations for reference measurement services for Urea, Uric acid, Glucose, Cholesterol in blood serum and plasma submitted by a calibration laboratory from Shanghai, China, and a nomination for a service for Glucose in blood serum/plasma /calibration solution from a calibration laboratory from Beijing.

There were two nominations for spectrophotometric-based reference measurement services for Urea and Glucose in calibration solution / blood serum, which were not being recommended for inclusion in the Database unless the Chinese laboratory corrects and restricts the applicable matrix to blood serum, considering that spectrophotometric-based methods for operating the services were not suitable for calibration solution samples.

The nomination for a reference measurement service for Creatinine in blood serum/plasma/calibration solution/high purity material operating the C14 RMP1 listed method was not accepted for inclusion in the Database unless the Chinese Calibration laboratory addresses the non-compliances. The DBWG recommended to exclude the calibration solution and high purity material in the description of the applicable matrices and to provide additional evidence (validation report) to support the extended concentration range declared by the laboratory service provider, or to revise the concentration range for consistency with the C14 RMP1 listed method.

The two remaining nominations for reference measurement services for Urea (using C7RMP26 listed method) and total Bilirubin in blood serum/plasma were not being recommended for inclusion in the database unless the service provider provides a validation report as evidence for the extended concentration range declared, or revises the concentration range, for consistency with the listed methods used to operate the services.

The DBWG noted the laboratory used a statistical approach to ensure traceability of its service given the primary calibrator for total Bilirubin NIST SRM 916a had been unavailable since 2015. It further recommended to defer the recommendation of the total bilirubin service until other laboratories with a listed service for bilirubin provide feedback on how they deal with the lack of primary calibrator and what calibrant they were using and how they manage traceability.

The Committee approved the DB WG's recommendation for Metabolites and Substrates nominations.

### **9.2.6 Non-Peptide Hormones [JCTLM-EXEC/19-08]**

There were 30 nominations for certified reference materials, two nominations for reference measurement methods and nine nominations for reference measurement services that have

been reviewed by the review team for Non Peptide Hormones, and of these 18 were being recommended for listing in the database.

### **Materials**

There were 30 nominations for high purity certified reference materials of steroid hormones and their derivatives (15 in a neat form and 15 ampouled materials) for which the producer submitted data/information and revised certificate to respond to non-compliances observed during last year review cycle. The DBWG recommended the listing of the materials in the neat form following the recommendation of the Drugs team.

However, major issues for ampouled materials concerning the statement about mass transferability, and assessment of homogeneity in the certificate still needed to be clarified by the producer before recommending the listing of the material.

### **Methods**

There was a first nomination for an isotope dilution LC-MS/MS based candidate reference method for the quantification of Androstenedione in human serum and plasma, which was not being recommended for listing in the database. Major non compliances concerning the lack of a formal publication of the paper supporting this nomination, incomplete interference study and missing independent assessment of trueness would need to be addressed and resolved prior resubmission to JCTLM.

There was a second nomination for a reference method for ID LC MS serum Estriol (non-conjugated), which was not being recommended for listing in the database. Major non compliances concerning the lack metrological traceability and purity determination of the calibrator as well as an incomplete interference study would need to be addressed and resolved prior resubmission to JCTLM.

### **Services**

There were nine nominations for reference measurement services submitted by four Calibration laboratories from China, and of these three services for Progesterone and Testosterone in serum /plasma and TT4 in serum /plasma/calibration solution were recommended for inclusion in the database.

The DBWG noted that four nominations were not being recommended for listing because the laboratory service provider claimed much lower concentrations than the acceptable ranges of the employed RMPs listed in JCTLM database, and additional validation report to support the extension of the measurement range to low concentration would need to be submitted to resolve this observed non-compliance.

The DBWG rejected two reference measurement services since the laboratory operates the procedure in a range with a large difference to the JCTLM listed values.

The Committee approved the DB WG's recommendation for Non Peptide hormones nominations.

#### **9.2.7 Nucleic acid [JCTLM-EXEC/19-09]**

There was a nomination for a reference method for Human cytomegalovirus quantification by dPCR for which the submitter has provided additional information/data in response to the non-compliances observed by the review team during last year's review cycle.

The DB WG recommended not to list this nomination until the scope of this submission was revised to be limited to purified gDNA. It also invited a new submission as a separate RMP with a broader scope but limited to sample matrix plasma where correction for recovery (and associated MU) would be accounted for as noted by the review team (to be consistent with the evidence supplied).

The Committee approved the DB WG's recommendation for Nucleic acid nomination.

### **9.2.8 Proteins [JCTLM-EXEC/19-10]**

There were four nominations for certified reference materials, three nominations for reference measurement methods and two nominations for reference measurement services that were reviewed by the Proteins team, and of these a method for Amyloid beta 1-40 in human CSF and a HbA1c service were being recommended for approval and publication in the JCTLM Database.

#### **Materials**

There were four nominations for certified reference materials for Alpha-fetoprotein, C-Reactive Protein and Leptin in buffer solution and for Troponin I in lyophilised products, and all of these were not being recommended for listing in the JCTLM Database. Critical non-compliances concerning the lack of commutability information and clarification of the material intended use statement would need to be addressed and resolved before resubmission to the JCTLM.

For the CRP material, a major issue regarding the material characterisation, and a critical element for clarification was the applicable traceability chain for the CRP material. These needed to be resolved prior resubmission to JCTLM.

#### **Methods**

There was a first nomination for a LC-MS method for measurement of Amyloid beta 1-40 in human CSF for which the nominating organization provided sufficient evidence to address most non-compliances observed during a previous review cycle in 2017 but required the provision of additional published documentation for listing in the JCTLM Database. The DBWG noted the review team's comment that elements required for review (calculation of uncertainty, some of the method validation, method used for characterization of the primary calibrator and acceptance of purity of calibrator) were not available in a publicly available document. It confirmed that this information must be either available as a document available through the JCTLM database or as a publication, for the method to be accepted into the JCTLM Database.

There was a second nomination for a LC-MSMS method for analysis of amyloid beta 1-40 in human CSF from another group which was a modification of the listed JCTLM method for quantification of the Abeta 1-42 peptide in CSF and was not being recommended for inclusion in the JCTLM Database. Major elements concerning the verification and quantification of the primary calibrator as well as the publication of the paper cited for the validation of the method would need to be addressed prior to resubmission to JCTLM.

The DBWG pointed out that as per the JCTLM-P04-B requirement, the comparability of the methods for amyloid beta 1-40 in CSF would need to be considered when the second group would resubmit their method to the JCTLM.

There was a third nomination for a IDMS RMP for Glycated albumin which was not being recommended for listing in the database. Critical elements for compliance with requirements in the ISO 15193 standard would need to be resolved prior to resubmission of the nomination to JCTLM.

### **Services**

There was a first nomination for a HbA1c reference measurement service from a Chinese calibration laboratory which was being recommended for inclusion in the database.

There was a second nomination for a Total Protein reference measurement service from a calibration laboratory operating the biuret procedure which was removed from the database in 2013. (This relates to the fact that Total serum protein, NRSCS RS5-A2 standard was no longer maintained in the consensus process by CLSI.) The EC agreed to place the method in the file for no longer listed methods with a reference to the paragraph 3 and Dumas' references 1 and 2 cited in NRSCS RS5-A2 together with reference to the calibrator used in the method.

The DBWG noted that Beijing Aerospace General Hospital Reference Laboratory, China and Instand, Germany offered the same service and referred to the same procedure in the database. It further recommended to defer the new service nomination until the biuret method for total protein can be nominated by any of the laboratories offering the service with a review performed before the next review cycle starts.

The Committee approved the DB WG's recommendation for Proteins nominations.

**Action (A/19-19):** Secretariat to contact laboratories having a service listed in the database for total protein, and invite them to nominate their method for inclusion in the JCTLM database

### **9.2.9 Vitamins**

There was one nomination for a reference measurement method of Vitamin D metabolites from blood spot and three nominations for reference measurement services for 25-hydroxy vitamin in serum/plasma from three Chinese services providers that were reviewed by the review team for Vitamins, and all of these were not being recommended for inclusion in the database.

**Action (A/19-20):** Dr Phinney to finalize the review reports for Vitamins method and services nominations by the end of January 2019.

The Committee approved the DB WG's recommendation for Vitamins nominations.

**Action (A/19-21):** Secretariat to publish the nominations recommended for publication in the JCTLM Database and send out the report on the outcome of the review to the nominating organizations.

The Executive also supported the recommendation of the DBWG to update the process employed by the review teams and the Secretariat would be tasked to contact nominators and request missing information required for review against the relevant ISO standards as per request from the review team leaders from the next review cycle.

**Action (A/19-22):** Secretariat to revise the text of the relevant procedure document to modify the process for informing the nominator of missing information required for review against the relevant ISO standard which would be routed via the Secretariat.

### **9.3 Update on IFCC EQAS results**

There was no report of the update on the IFCC EQAS Scheme and RELA results.

#### **9.3.1 Accreditation status update**

Ms Bednarova pointed out the need to verify that the versions of the international standards referenced to in the JCTLM procedures documents with regards to the accreditation requirements of EQAS were still in use. The Committee invited her to become a member of JCTLM Quality System Review team. It further requested that a systematic review of the JCTLM Quality procedures documents be conducted in 2020 in order to verify the version of the standards referenced by JCTLM and anticipate any modifications would be required notably in relation to risk based approach adopted in newer standard.

**Action (A/19-23):** Ms Bednarova/Quality System Review team to revise JCTLM procedures documents for consistency with the up-to-date version of the standards and draft proposal for modifications for new EQAS requirements for discussion at the next Executive Meeting in December 2019.

### **9.4 Progress/ plans for Cycle 17 for RMs and RMPs and Cycle 15 for RMSs**

In accordance with the generic time schedule of the JCTLM review cycle, it was agreed that the next call for nominations for Reference Materials, Methods, and Services would be launched on the 1st of February 2020 with a deadline for submissions in May 2020.

## **10. Outcome of the mini-workshop ‘Working together towards Standardization in Laboratory Medicine – co-ordination of international activities’**

Dr Myers said that the mini-Workshop was an excellent opportunity to bring together experts from various professional fields, and a written report of the outcomes of the groups’ discussion would be produced from inputs of the participants and distribution at the beginning of next year. This would be the basis for producing an international roadmap describing how international and national organizations can work together most effectively in a coordinated way to promote comparability of results in laboratory medicine.

## **11. Update on gap analysis study**

Dr Jones recalled that the latest update of gap analysis of the missing reference materials, methods and services listed in the database, with regards to the frequently requested measurements made in his clinical laboratory, as well as the widely used measurement services provided by the Australian EQAS for routine laboratory was conducted in June 2016, and published in the JCTLM Newsletter in 2017. He questioned whether this exercise has had any impact and should be continued. The Committee said that the gap analysis had been useful for the actors involved in the standardisation in laboratory medicine. It further added that this project should be continued to investigate the impact of the JCTLM standardisation activity and need for improvements based on the EQAS results worldwide looking at the most commonly used tests in Medical laboratories.

**Action (A/19-24):** Dr Jones to conduct a JCTLM database gap analysis describing complete and not complete reference measurement systems listed in the JCTLM Database to highlight

where improvements would be required based on commonly used tests in Medical laboratories, and to consult with the TF-RMSI, as there may be some overlap in activities.

## **12. Liaison with ISO TC 212**

Dr Wielgosz reported that Dr Hubert Vesper would be the new convenor of the ISO TC 212 WG2 starting from January 2020.

### **12.1 Update of revision of ISO 17511:2003**

The document FDIS of the revised text of the ISO 17511 on the requirements for establishing metrological traceability of values assigned to calibrators, trueness control materials and human samples was being registered and the publication of the IS was expected in April 2020.

As discussed before, the publication of the new international standard ISO/DIS 21151 on the requirements for international harmonization protocols establishing metrological traceability was submitted in parallel and expected also in April 2020.

### **12.2 Other work items in ISO TC 212**

The document ISO/TS 20914 Medical laboratories — Practical guidance for the estimation of measurement uncertainty was published in July 2019.

. A future joint project with ISO/TC212/WG1 to support measurement uncertainty requirements in ISO 15189:2012 was anticipated at the time of the systematic review of the Technical Specification. At that time, it would be necessary to anticipate the renewal for 2nd 3-year term, or conversion of the TS to International Standard.

The systematic revision of ISO 15193:2009 and 15194:2009 would be initiated in January 2020.

## **13. Liaison with the EC**

The Committee recognized the importance of approaching Notified Bodies with responsibility for the implementation of the EU IVDR and raise awareness of the service provided by JCTLM;

**Action (A/19-25):** Dr Myers to draft a pamphlet for regulators on traceability and explaining JCTLM and its services available.

## **14. Liaison with the WHO**

This agenda point was discussed under 2.1.

## **15. Reports related from related activities/meetings**

### **15.1 Report for the IFCC SD meeting**

There was no report submitted.

### **15.2 IFCC World lab meeting in Seoul 2020**

Dr Jones informed the Committee that in addition of the JCTLM session on metrological traceability in laboratory medicine, a session lead by IFCC SD on the challenges and opportunities of the standardisation in laboratory medicine would be held during this conference.

## **16. Future meetings of the JCTLM**

### **16.1 JCTLM Members and Stakeholders meeting in 2021**

The Committee confirmed the 6 and 7 December 2021 as the dates for the next JCTLM Members' and Stakeholders' meeting, and the venue would depend from the results of the study of the cost and options for hosting workshop with larger attendance. This would be followed by a TEP-WG meeting on 8 December (morning), and a Database WG meeting on 8 (afternoon) and 9 (morning) December as well as a JCTLM Executive meeting on 9 and 10 December 2021 at the BIPM.

### **16.2 JCTLM events in 2020 and 2021**

It was also agreed to either hold an Executive meeting in conjunction of the IFCC World lab in Seoul or alternatively a teleconference meeting of the Executive Committee in May 2019 for reviewing any action items of this meeting.

The Committee confirmed that the Database WG meeting would be held on 2 December and 22<sup>nd</sup> Meeting of the JCTLM Executive Committee on 3 and 4 December 2020.

Dr Wielgosz said that the third edition of the international conference on research and quality assurance on Therapeutics and Diagnostics was being organized by NIM (China), NIFDC (China) and would be held on 13-15 July Nanjing, Jiangsu, China.

Mr Fawcett informed the Committee that the General Assembly of the ICSH would be held in Singapore on 14/15 October 2020, and invited JCTLM Executive representatives (Dr Liu, HSA, Singapore) to attend and present the JCTLM acceptance criteria and review requirements and pitfalls with the case study close from haematology.

## **17. JCTLM instructions for industry use**

Dr Jones recalled the document [JCTLM-EXEC-15-03](#) provided advice to manufacturers and others on the appropriate manner to make reference to JCTLM-listing of reference materials, methods and services in any documentation in which information on metrological traceability was included. He pointed out that these instructions could be revised along with the release of new ISO 17511 and questioned the possibility of developing a process for use and application of JCTLM logo by third parties.

**Action (A/19-26):** Dr Jones to review the JCTLM Instructions for use and draft a proposal for a process for use and application of JCTLM logo by third parties.

## **18. Close**

The Chairman closed the meeting on 6 December at 13:00.

## Annex 1: Summary List of Actions

### **Actions from the 21st Executive Meeting:**

**Action (A/19-01):** Secretariat to contact members of review teams regarding completion/or reappointment of their 5 year terms as review team members, and access to the ISO Standards.

**Action (A/19-02):** Dr Wielgosz to develop a plan and scope for a training project on ISO Standards.

**Action(A/19-03):** RELA advisor to confirm the adequacy of the evidences provided by the service laboratory to fulfill JCTLM criteria in relation to its participation in the EQAS Scheme for 2015-2017.

**Action (A/19-04):** IY/RW to draft a procedure for accession and termination of JCTLM Executive Member Status which is referred to in the DoC for discussion at the Executive Meeting in December 2020.

**Action (A/19-05):** BIPM to draft a procedure for an induction process for new EC members of JCTLM Executive Member Status for discussion at the Executive Meeting in December 2020.

**Action (A/19-06):** Secretariat to post JCTLM Member organizations' activity reports on the BIPM JCTLM Members dedicated webpage.

**Action (A/19-07):** JCTLM Secretariat to draft technical specifications for updating the JCTLM Database web system and application and launch a call for tender.

**Action (A/19-08):** Secretariat to modify the relevant procedure documents to include a clause on conflict of interest and confidentiality which would be applied during the review process.

**Action (A/19-09):** SM/MB to review JCTLM quality procedures including JCTLM rules for regular participation in EQAS Scheme

**Action (A/19-10):** SM/RW/QL/MQ/KP to revise the procedure document P04-A to propose a model taking into account the comparisons performed within the framework of CIPM MRA, the type of analyte for which the well-established CCQM system could be employed to demonstrate equivalence, and also the number of materials that would be required for a comparability study.

**Action (A/19-11):** JCTLM Chair to draft a proposal for JCTLM Workshop on Commutability at EuroMedlab Meeting in 2021 in Munich

**Action (A/19-12):** JCTLM EC members to review new standard ISO 21151 to highlight what information would be suitable for publication in the JCTLM Database, for discussion during a conference call.

**Action (A/19-13):** Secretariat to investigate the cost and the options for hosting the next Workshop to larger capacity venue outside the BIPM.

**Action (A/19-14):** Prof Panteghini to recruit further members for the TF-RMSI to carry out an additional study.

**Action (A/19-15):** Secretariat to contact Proteins review team to provide a complete dossier with information concerning the reviews of the CDT Method and their decision to maintain their recommendation for requesting corrective action for consideration by the EC

**Action (A/19-16):** Secretariat to contact the Drugs review team to provide a complete dossier with information on the review of the Sirolimus material in blood and the recommendation from the review team in regard to the producer's response appealing the EC recommendation, for consideration by the EC

**Action (A/19-17):** EC to amend the review report of the ICSH outstanding method in accordance with the EC recommendation.

**Action (A/19-18):** EC to liaise with Blood cell counting team in order to review the team membership and to resolve the review of the erythrocyte method

**Action (A/19-19):** Secretariat to contact laboratories having a service listed in the database for total protein, and invite them to nominate their method for inclusion in the JCTLM database.

**Action (A/19-20):** Dr Phinney to finalize the review reports for Vitamins method and services nominations by the end of January 2019.

**Action (A/19-21):** Secretariat to publish the nominations recommended for publication in the JCTLM Database and send out the report on the outcome of the review to the nominating organizations.

**Action (A/19-22):** Secretariat to revise the text of the relevant procedure document to modify the process for informing the nominator of missing information required for review against the relevant ISO standard which would be routed via the Secretariat.

**Action (A/19-23):** Ms Bednarova/Quality System Review team to revise JCTLM procedures documents for consistency with the up-to-date version of the standards and draft proposal for modifications for new EQAS requirements for discussion at the next Executive Meeting in December 2019.

**Action (A/19-24):** Dr Jones to conduct a JCTLM database gap analysis describing complete and not complete reference measurement systems listed in the JCTLM Database to highlight where improvements would be required based on commonly used tests by Medical laboratories, and to consult with the TF-RMSI, as there may be some overlap in activities.

**Action (A/19-25):** Dr Myers to draft a pamphlet for regulators on traceability and explaining JCTLM and its services available

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