Report of the 11th meeting of the JCTLM Executive Committee
6-7 December 2012, BIPM, Sèvres, France

List of participants:
Prof. M. Müller (JCTLM Chairman, IFCC)
Dr R. I. Wielgosz (JCTLM Executive Secretary, BIPM)
Dr G. Beastall (IFCC)
Mr A. Squirrell (ILAC)
Dr G. Jones (ILAC)
Dr R. Kaarls (CIPM)
Prof. M. Kühne (BIPM)
Dr. M. Milton (BIPM)
Prof. L. Siekmann (IFCC, JCTLM WG 2 Chair)
Dr H. Schimmel (JCTLM WG1 Chair)
Dr S. Maniguet (JCTLM Secretariat, BIPM)

Apologies received:
Prof. L. Thienpont (JCTLM WG 2 Chair)
Dr K. Phinney (JCTLM WG1 Chair)
Dr W. E. May (CIPM)

Prof. Müller opened the meeting, and welcomed Dr Milton Deputy Director of the BIPM to the meeting.

1. Approval of the agenda [JCTLM-EXEC/12-01]

Dr G. Jones asked for an additional agenda point to be added to allow for discussion on clinical traceability. Prof. M. Müller agreed that this general discussion should be dealt with under the agenda point 14.2.

2. Report of 10th JCTLM Executive Committee Meeting

There were no comments on the report of the 10th Executive Committee meeting, which had been finalized in March 2012, and published on the BIPM JCTLM website.

2.1 Review of action points arising from the 10th meeting [JCTLM-EXEC/12-02, 24]

Dr Wielgosz summarized the action items that were still outstanding:

Action (A/11-01): WG1 Chair/Dr Phinney to contact D. Bunk to clarify whether or not the HbA1c materials and methods should be re-reviewed or remain listed.
Action (A/11-03): Prof Siekmann to prepare a short discussion paper for the Executive outlining the current status of primary calibrators for HbA1c.
These two actions were completed during the closed meeting on HbA1c reference measurement systems that was held on 14 July 2012 and reported in the document JCTLM-EXEC/12-04.

Action (A/11-04): Dr Phinney to coordinate discussions within CCQM OAWG on the use of RELA samples for relevant CCQM comparisons

Prof Siekmann reported that there had been no requests from national metrology institutes for RELA samples during the last year. The Committee requested that the Chair of the CCQM OAWG should be contacted to verify it would be possible that the coordination on the use of RELA sample for relevant CCQM study be addressed at future OAWG meetings.

Action (A/11-05): JCTLM Secretariat to circulate the revised text for the Declaration of Cooperation (DoC) amongst the three sponsoring organizations for their approval, and to follow up the action A/10-06 to inform the JCTLM member organizations of their obligations, and that they would need to report regularly (every 2 years) on their activity in support of the JCTLM.
This issue will be dealt with under agenda point 3.1.

Action (A/11-12): Prof. Siekmann to draft a paper addressing the issue on the use of the concentration versus the mass fraction.
Prof. Siekmann reported that this issue had been addressed during the last WGs meeting. In the discussion that followed, some members of the Committee pointed out that further guidance was needed for CRM users to clarify all the uncertainty contributions that have to be taken into account for the conversion of a mass fraction value stated in the certificate to a concentration value. The Committee requested that a draft proposal be discussed during the next WGs meeting based on the review of the information that was available in the certificates of analysis.

Action (A/11-13): JCTLM Secretariat/Prof Thienpont to review the analyte names in the database to improve the consistency of the information provided to the user.
Dr Wielgosz reported that the list of the analyte names entered in the database together with their corresponding EC/CAS numbers had been sent out to Prof Thienpont for her review, and that the database would be updated according to the corrections she would propose.

Action (A/11-14): Dr Beastall to draft the aims and structure of a possible study on the impact of metrological traceability in laboratory medicine and clinical chemistry.
Dr Beastall reported that further investigation would be needed to select the target measurand for the impact study of metrological traceability, and to anticipate the financial resources required for that exercise. Some members of the Committee pointed out that a collaborative impact study on metrological traceability could be investigated at a national level.

Action (A/11-16): The Executive Committee to comment on the document JCTLM EXEC/10-31 by the 15th of January 2012
This will be dealt with under agenda point 7.

Action (A/11-17): JCTLM Secretariat to contact CDC to verify if they wish to withdraw their Abel-Kendall reference measurement method for Cholesterol from the JCTLM database after publication of their improved method
Dr Wielgosz reported that CDC had been contacted, and that they do not wish to withdraw their Abel-Kendall method from the JCTLM database. The Executive Committee expressed their concerns of having two co-existing reference measurement systems for Cholesterol listed in the database that would give two different measurement results. Prof Siekmann added that the Abel-Kendall method based on a colorimetric principle had shown a lower specificity compared to the IDMS method. He requested that a comparative study be organized using patient samples.

The Committee agreed that the issue raised on the difference observed for the specificity and the measurement result value between both listed methods should be addressed to the CDC in January 2013 before taking any further corrective actions.

Action (A/11-22): JCTLM Secretariat to clarify the issue of the purity of the primary calibrator with the nominator of the triglycerides reference measurement service
Dr Wielgosz reported that the laboratory had been contacted, and their response to the Review team's question on the purity of the primary calibrator used for their triglycerides reference measurement service was currently being reviewed by the review team.

Action (A/11-25): Dr Jones to distribute the draft of the position paper for contributors' comments by the 15th of February.
The paper on history and function of the JCTLM will be dealt with under agenda point 7.

Action (A/11-27): Prof Müller to contact Prof Panteghini to see if a JCTLM Stakeholder meeting can be scheduled in conjunction with the EUROMEDLAB 2013 meeting.
Prof Müller reported that it was not possible to organize a JCTLM Stakeholder meeting at the occasion of the EUROMEDLAB 2013 meeting due to the passed deadlines for submitting the proposals.

New Actions:
Action (A/12-01): BIPM to contact the Chair of the CCQM OAWG in order to verify the possibility to address the issue of the use of RELA samples for relevant CCQM comparisons as a permanent item agenda future OAWG meetings.
Action (A/12-02): BIPM/NIST to review the information available in the NIST SRM certificates of analysis, and to draft guidance on the correction factors that CRM user would need to apply for the conversion of mass fraction to concentration values for discussion at the next WG meeting
Action (A/12-03): JCTLM Secretariat to liaise with CDC to inform them on the need to clarify to the database user if there were differences in the measurement results obtained in using Abel-Kendall or their improved IDMS method, and to verify the feasibility of a comparative study including patients' sample and spiked steroid samples.

3. JCTLM Framework and Declaration of Cooperation

3.1 Modified text for Membership Obligations and Privileges

Dr Wielgosz reported that the revised text of the Declaration of Cooperation (DoC) between the CIPM, IFCC and ILAC, and of its Appendices III and IV had been approved by the three sponsoring organizations, and would be posted on the BIPM JCTLM website at the beginning of next year. He added that the action A/10-06 would be followed up to inform the JCTLM member organizations of their obligations, and that they would need to report regularly (every 2 years) on their activity in support of the JCTLM.

3.2 Representation on the Executive

Dr Wielgosz informed the Committee that the Secretariat had contacted the sponsoring organizations, the IFCC, the ILAC and the BIPM for nominations of JCTLM Chairman and Secretariat. The nomination of Prof M. Müller from the IFCC was received for JCTLM President, and no nominations for the Secretariat were received.

The JCTLM Executive approved the re-appointment for the next two years of Prof M. Müller as Chairperson, and the BIPM's continued role as Secretariat for the JCTLM.

3.3 JCTLM membership [JCTLM-EXEC/12-28]

Dr Wielgosz informed the Committee that one organization had applied for membership of the JCTLM, the National Metrology Institute from Turkey - Ulusal Metroloji Enstitüsü (UME). The Committee reviewed the application JCTLM-EXEC/12-28 and approved the JCTLM membership of UME.

Actions:
Action (A/12-04): JCTLM Secretariat to write to UME to confirm the Executive's approval of membership.

3.4 JCTLM Working Groups

3.4.1 Review of JCTLM Review Teams and RT Members [JCTLM-EXEC/12-06]

Dr Wielgosz reported that the Secretariat had informed the review team leaders that the term for membership of five years renewable was applicable from January 2012, and had requested them to confirm the list of their review team members. Eleven of the thirteen review team leaders have sent feedback, and amongst them eight have confirmed formally the list of the members of their review team, and three have requested some modifications in the list of the members of their team.

The list of the members of the review teams were formally confirmed for Blood cell counting, Coagulation Factor, Drugs, Enzymes, Non electrolyte metals, Non peptide hormones, Proteins for WG1 and WG2, as well as for Quality systems for WG1.
It was noted that two review team leaders for Drugs and Non peptide hormones had decided to keep all the members of their team, although they have had no feedbacks from Dr Jones (USP) for Drugs nominations and Dr Bei (NIM) for Non peptide Hormones nominations during the last review cycle.
The leader of the review team for Coagulation factors had also informed JCTLM that all members of the team had met during the year and were planning to meet in the short term to discuss the nominations for new submissions.

The review team leader for Microbial Serology had informed JCTLM that Ian Sharp from the Health Protection Agency in United Kingdom was no longer willing to be a member of the team. Although the team was left with its leader only, the Committee decided to keep the team in place with its current composition given that there were no issues and requests for the review of microbial serology nominations.

Dr Sharpless had informed JCTLM in the document [JCTLM-EXEC/12-06] of her resignation as leader of the Vitamins and Micronutrients review team, and had proposed to nominate Dr Wiebe as candidate for WG1 & WG2 Vitamins and Micronutrients review team leader position, and to remain a member of the review team.

Dr Welch had written an email to inform JCTLM of his resignation as leader of the Metabolites and Substrates review team on 1st of January 2013, and had proposed to nominate Dr Bei as candidate for WG1 & WG2 Metabolites and Substrates review team leader position. He had received a confirmation from four members of the review team of their willingness to continue to participate in the review team activity. He could not confirm the membership for

Steve Wolf (Beckman Coulter, Inc.) and Hanspeter Andres, (METAS) with no responses from them to his emails, and has proposed to withdraw Norihiko Kayahara (Kyowa Medex Co., Ltd.) who could not be reached anymore.

No confirmations or requests for modification were received from the Blood groupings, Electrolytes, and Nucleic acid review teams.

The Committee approved the modifications proposed for the list of members of the review teams for Microbial Serology, Vitamins, and Metabolites and Substrates, and appointed Dr Wiebe as leader of the WG1 &WG2 Vitamins review team, as well as Dr Bei as leader of the WG1 & WG2 Metabolites and substrates review team with the assumption that she would respond to email from the Non-peptide hormones review team leader.

The Executive Committee pointed out the need to investigate the status for the reference measurement systems for Blood Gases, and requested that the experts in this field and members of the Electrolytes and Blood gases review team be contacted.

The Executive Committee thanked all Review Team Leaders and Members that were stepping down for their contributions to the work of the JCTLM, which had been essential to its success.

Actions:
Action (A/12-05): Dr Schimmel to contact Dr Bei to clarify if she would continue to contribute to the Non-peptide Hormones review team activity, and to confirm if she would be eligible as Leader of the Metabolites and Substrates review team
Action (A/12-06): Secretariat to update the list of review team leaders and members, and to contact new review team leaders informing them of their approved nominations
Action (A/12-07): WG1 and WG2 Chairs to contact the Blood gases experts of the review team to verify the current status of higher metrological order items for Blood gases reference measurement systems.

3.4.2 Review Team Scope of activities [JCTLM-EXEC/12-05]

Dr Maniguet introduced the document [JCTLM-EXEC/12-05] covering the terms of reference for the review teams which had been drafted by Dr C. Jackson and had been finalized to include all the review teams' comments with the exception of those of the nucleic acids' group for which there were three proposals.

Dr Schimmel commented that the traceability statement at the end of each paragraph for each group of analytes would need to be deleted as this had been already discussed in previous email exchanges between review team leaders. He added that he had the opportunity to comment the ToRs for the nucleic acid review team and that they had reached an agreement on the final version for the terms of reference for nucleic acid team.

The Committee asked Dr Schimmel to contact Dr Jackson and the Nucleic acid review team to finalize the terms of reference document.

Action
Action (A/12-08): WG1 Chair/Dr Schimmel to contact Dr C. Jackson to correct the pending issue for the traceability statements and to finalize the nucleic acid review team terms of reference, and to circulate the final version for approval by the Executive Committee.

3.5 Funding of the JCTLM Secretariat

Dr Wielgosz reported that the invoice which was sent in November 2012 to the IFCC was based on the time sheet record in use at the BIPM. The operating costs of the JCTLM Secretariat included the tasks related to the organization of the JCTLM Executive meeting and related documentation, the processing of JCTLM submissions and reviewed nominations, the development and the maintenance of the JCTLM Database, the activity for liaison with external organizations related to the JCTLM, the organization and attendance of the WGs' meetings and the drafting of the meeting reports. The effective cost for 2012 JCTLM Secretariat appeared to be in line with that foreseen and presented in the document JCTLM-EXEC/10-24 which was the financial support required for the JCTLM Secretariat activities for 2011 to 2015 that was produced based on that of 2010 with an increase of 2% per year for inflation.

Dr Wielgosz reminded the members of the Committee that the resources and the costs of JCTLM Secretariat had been shared equally between the BIPM and the IFCC since 2004, and that the BIPM's budget was fixed until 2015 and based on the continued sharing of costs for this activity. The BIPM budget for the four year period starting in 2016 would be set at the next General Conference for Weights and Measures to be held in October 2014.

Dr Beastall stated that the IFCC was under financial pressure and wished to discuss alternative funding mechanisms. The BIPM requested that any change in funding the activity should be introduced progressively, so as to allow sufficient time for an alternative funding structure to be put in place to support the essential work carried out by the JCTLM Secretariat. Dr Beastall confirmed that the IFCC would continue to fund half of the operating costs for the JCTLM Secretariat as foreseen until 2015, provided that the discussion on alternative funding structures was started next year, as it was likely that the IFCC financial plan from 2016 onwards would not allow its contribution to remain at the level of previous years.

In the discussion that followed, the JCTLM Committee agreed that the issue of funding JCTLM Secretariat activities would need to be included during the JCTLM Stakeholders meeting in 2013, and requested that in the meantime a paper be drafted on the future structure, funding, and impact of JCTLM.

Actions:
Action (A/12-09): Dr Schimmel, Dr Beastall, Dr Wielgosz, Dr Jones to draft a paper for next JCTLM Executive Meeting on the future structure, funding, and impact of JCTLM

3.6 JCTLM Database

Dr Maniguet presented the updates of the JCTLM Database that were completed in 2012. In January 2012, twenty-four reference measurement services from 2 reference laboratories that were still undergoing accreditation had been temporarily removed from the JCTLM lists. These services would be reinstated after receipt of the copy of the laboratories' accreditation certificates for compliance with ISO 15195 and ISO/IEC17025 as calibration laboratories. Additionally, eleven services from one of the laboratories which had been accredited were reinstated in July 2012.

In March 2012, thirty-four entries for certified reference materials, 5 for reference measurement methods and 1 for a reference measurement service were published in the

JCTLM Database following the approval by the Executive Committee of nominations reviewed during WG1 cycle 8 and WG2 cycle 6.

In April 2012, one CRM which was no longer available for sale was placed in the PDF file of the "List of reference materials no longer available in the JCTLM database" that can be downloaded from the JCTLM database website.

In June 2012, 210 reference materials listed in the JCTLM database which had not been resubmitted for re-review for compliance against the revised standard ISO 15194:2009 by the deadline of 31 May 2012, were annotated in the database to inform the user that the material had been reviewed for compliance with ISO 15194:2003.

The current status of the database as of December 2012 was as follows:
- 262 certified reference materials (CRMs) amongst which 33 are in List II (i.e. Reference Materials value assigned using an internationally agreed protocol), and 3 are in List III (i.e. Reference Materials for nominal properties),
- 157 reference measurement methods covering 76 analytes, and
- 74 reference measurement services covering 32 analytes. These services are delivered by 8 reference laboratories accredited for compliance against ISO 15195 and IEC/ISO 17025 as a calibration laboratory, and by 1 National Metrology Institute (NMI).

The content management system and the web system of the database had been modified to allow the download of all entries for materials, methods or services in a PDF format, and this new functionality had been made available in November 2012.

The Committee pointed out that the listed accredited reference laboratories were almost all from Europe, with only two from other parts of the world.

Mr Squirrell commented that it would be difficult to take further action in the countries where the accreditation was not required by regulatory bodies, and in the case where standardization relied on well-established Networks of laboratories.

Prof Siekmann added that he was aware of a small number of Accreditation bodies in the Asian region that could offer the accreditation service in comparison with the increasing number of reference laboratories which had been participating in the RELA Scheme, notably from China.

Dr Wielgosz added that the ISO 15195 was not currently in the list of harmonized standards related to the IVD Directive that would make a difference for compliance with the requirement.

The Committee concluded that JCTLM should liaise with laboratories from recognized Laboratory Networks , and requested that ILAC contact its member organizations to verify the current status for accreditation service notably in North America or in China.

Actions:
Action (A/12-10): JCTLM Secretariat to liaise with network laboratories with regards to the accreditation issue of the laboratories participating in the Network

Action (A/12-11): ILAC to contact Accreditation Bodies to confirm whether or not they are able to offer an accreditation service to ISO 15195, for updating the list on the JCTLM website

4. Outcomes of JCTLM Meetings (July 2012)

4.1 Outcomes of the JCTLM WGs meeting, July 2012, Los Angeles US [JCTLM-EXEC/12-03, 07]

Dr Wielgosz presented the document JCTLM EXEC/12-03 which described the issues and actions raised during the discussions with WGs in July, and the document JCTLM EXEC/12-07 which included the list of items that were received from the database user feedback web form, and which was communicated to IFCC for evaluation.

The following outstanding issues were discussed:

Action (A/WG-12-01): G. Beastall to contact the editor of the CCLM journal to see if it would be possible to create a new e-service for the publication of reference methods and validation data.

Dr Beastall informed the members of the Committee that the CCLM journal would cease publication in 2013, and that the IFCC was currently considering other publisher's for its journal, and that discussions on a new e-service publication would be delayed until this was settled.

Dr Wielgosz asked whether or not it would be possible to publish the publications on methods in the e-Metrologia in a similar way to the service that was offered for the publication of the results for CCQM inter-laboratory comparison results. Dr Milton replied that the BIPM would contact the board of Metrologia to see if it would be possible to expand their electronic service to respond to the need for publications of modified, improved or newly developed reference measurement methods to support metrological traceability in the field of laboratory medicine and clinical laboratory.

Action (A/WG-12-02): JCTLM Secretariat to contact the producers of reference materials having not yet re-submitted their reference materials for compliance with the revised standard.

This action was not completed, and was pending the drafting of a comparison table to clarify what were the key differences between both versions of the standard ISO 15194.

Action (A/WG-12-03): JCTLM RT for Quality Systems to draft a comparison table to clarify what were the key differences between both versions of the standard ISO 15194 that have been used by the JCTLM review process.

The document JCTLM-EXEC/12-08 which was drafted by Dr Jackson, and had been circulated for comments to the review team leaders was presented in the next agenda point 4.1.1.

Action (A/WG-12-04): JCTLM/AACC to see if it could be possible to set-up webinars, AACC training courses and satellite meetings at the occasion of the AACC annual meeting in order to address these JCTLM issues to a larger IVD /laboratory medicine community.

Dr Wielgosz reported that this action had not been undertaken, and that the BIPM currently did not have the infrastructure to run webinars. However, a discussion on the future

development of electronic meeting media had started at the BIPM together with an assessment of the resources that would be required to put this in place.

Action (A/WG-12-09): WG1 Chairs to discuss with the review team leaders to see if they were willing to change the rules and allow for a transition period to get finalized supporting documentation, and prepare a proposal for the Executive meeting.
Dr Schimmel explained that the decision to review nominations for which the supporting documentation was finalized late in the review process had been left to the review team leader over the previous review cycles. He added that at a correct balance was needed for the time given to nominators to prepare their submissions and the time given to the review teams to complete their review. He proposed that the deadline for submitting completed nominations should remain the 30th of May, and that the deadline should be extended to the 30th of September to allow organizations to submit the final version of supporting documentations in a non-changeable format. The Committee agreed with the proposal and requested the modification of the JCTLM procedures.

Action (A/WG-12-11): G. Beastall to circulate this list of proposed items to the IFCC SD for review and comment, and reporting to the JCTLM Executive.
Dr Wielgosz reminded the committee that the feedback user form was developed to identify the specific/potential needs and concerns regarding materials, methods or laboratory services in the field of laboratory medicine, and that the WGs recommended that the list of items [JCTLM-EXEC/12-07] suggested by the user of the JCTLM database would best be reviewed by the IFCC which had already a prioritization procedure /check list that could be used for this type information.
G. Beastall reported that the IFCC SD had considered the list of items during its meeting in November 2012 but was not able to draw any conclusions from it, with the exception that a number of the suggested measurands were already under development.

Dr Wielgosz asked the IFCC SD representatives whether or not it would be of any interests in the future to continue gathering such information? It was agreed that the feedback user form would be kept online on the JCTLM database website, and that the suggestions be forwarded to Dr Schimmel to inform IFCC SD of any major updates.

Action (A/WG-12-13): IFCC/BIPM to discuss the organization of a clinical chemistry and CCQM joint workshop on commutability.
Future meetings of the JCTLM will be discussed under agenda point 14.

New Actions:
Action (A/12-12): BIPM to contact the board of Metrologia to see if it would be possible to expand their electronic service to the publication of reference measurement methods in support of the metrological traceability for laboratory medicine community.

Action (A/12-13): JCTLM Secretariat to modify the JCTLM procedures to include the deadline of the 30th of September by which an organization would have to submit the final version in a non-changeable format of the supporting documentation in order to complete the nomination that would have been submitted by the 30th of May of the same year.

4.1.1 Comparison of ISO 15194:2002 vs. ISO 15194:2009 [JCTLM-EXEC/12-08]

Dr Wielgosz presented the document JCTLM EXEC/12-08 which compared the ISO 15194:2002 versus ISO 15194:2009. The old version of the standard had concentrated on the

description of higher order CRMs, whereas the new version now included requirements related to their production, value assignment and supporting documentation. ISO Guides 34 and 35 were normative references in the revised standard, and the need for consistency between the commutability statement and the scope of applicability of the material was emphasized.

He reminded the Committee that about 80% of the listed reference materials in the JCTLM Database were annotated as having been reviewed for compliance with the ISO 15194:2002 standard and not with ISO 15194:2009, and that the WGs agreed that a process for the re-reviewing annotated materials was needed to respond to requests from the IVD industry as to the status of these materials.

From the extensive discussion that followed, the Committee concluded that the re-review of CRMs was strongly encouraged but would not be required by JCTLM as the CRM user would be able to verify the compliance of the CRM with ISO Guide 34 requirements and the consistency between the commutability statement and the intend use stated in the certificate of the CRM.

Actions:
Action (A/12-14): JCTLM Secretariat to draft a statement on the differences between both versions of the ISO 15194 standard, and indicate that for reference materials reviewed against ISO 15194:2002, verification of the CRM certificate was required to determine the compliance of the CRM with ISO Guide 34 requirements and the consistency between the commutability statement and the intend use stated in the certificate of the CRM .

4.1.2 JCTLM Frequently Asked Questions [JCTLM-EXEC/12-09]

Dr Wielgosz introduced the document JCTLM EXEC/12-09 which was drafted by Dr Jackson, and included Frequently Asked Questions. The first set of questions/answers was for laboratory professionals and companies in laboratory medicine, and the second set of questions/answers was drafted for material producers and method developers.

Actions:
Action (A/12-15): JCTLM Secretariat and Dr Jones to review the document with Dr Jackson and circulate the new version to the members of the Executive Committee for comment.

4.2 Outcomes of the JCTLM meeting on HbA1c [JCTLM-EXEC/12-04]

Dr Wielgosz presented the document JCTLM EXEC/12-04 which described the decisions and actions from the JCTLM Workshop that was held in July 2012 to clarify the traceability issues regarding HbA1c reference measurement system items listed in the database.

The Committee reviewed the draft for the updated list of HbA1c methods which included the changes decided during the meeting in July. The IFCC HbA1c method was reformatted as two separate entries in the JCTLM database reflecting the two different methods using HPLC/ CE and HPLC/MS-ESI. The measurand information was added for the NGSP DCCT and IFCC reference methods, as well as the reference to the Master Conversion Equation for relation between the IFCC numbers and the respective national Designed Comparison Methods. The Committee reviewed the remaining separate entry for the Instand method and its corresponding reference: Kaiser P. et al. Modification of the IFCC reference measurement procedure for determination of HbA1c by HPLC-ESI-MS, *GMS Ger. Med. Sci.*, 2006, Doc. 06. It was pointed out that the measurand was expressed as a mass ratio in percent in the

procedure published by Instand, whereas the measurand of the IFCC method was expressed as an amount-of-substance of [HbA1c/(HbA1c+HbA0)] in nmol/mol. The Committee concluded that the measurand issue would need to be clarified and that the Instand entry would need to appropriately linked to the IFCC HPLC/MS-ESI method published in 2002, in order to be consistent with the fact that this was an update of the IFCC method which was used by the IFCC HbA1c Network laboratories. The Committee requested the Secretariat to add the reference published 2006 with a comment to clarify to the user that it was an update of the IFCC method published in 2002, and it that was currently used by the IFCC HbA1c Network laboratories.

The following outstanding action items were summarized:

2) G. Beastall to consult on the IFCC process to be followed to designate the method published by INSTAND (2006) as an IFCC designated method and verify if the IFCC approved reference measurement method using the LC-ESI-MS principle published in 2002, should remain listed in the JCTLM database.

Dr Beastall reported that the process for a method to be designated as IFCC method would require an IFCC SD decision. He confirmed that the IFCC approved reference measurement method based on HPLC-ESI-MS that was published in 2002 would remain listed in the JCTLM database.

3) Dr Kaiser and the IFCC Network to undertake further investigations on the origin of differences between the INSTAND (2010) method and currently published reference methods for HbA1c, and based on the conclusions of these investigations decide how to proceed with the outstanding reference method nomination to the JCTLM database.

The review of the nomination submitted by Instand for the IDMS method published in 2010 remained deferred.

4) H. Schimmel (IRMM) to send an email of confirmation to the JCTLM Secretariat requesting the removal of the BCR 405 reference material from the JCTLM Database and any comments that should be included in the file of no longer listed Reference Materials.

Dr Schimmel reported that he would write to the JCTLM.

5) Dr Umemoto (ReCCS) to provide further information on the JDS Lot 2 reference material for HbA1c for review by JCTLM WG1 / Review Team for Proteins; information to include explanations of the quantity, units and the method to which the values are traceable.

ReCCS had not sent any complementary information on the Lot 2 reference material for HbA1c after the meeting. The Executive asked the Secretariat to contact the producer to request the information as well as the JCTLM submission file for appropriate review by JCTLM team. Failure to provide this information would result in the delisting of the reference material.

10) IFCC Network /IRMM are invited to develop and publish the methods used for the value assignment of pure HbA1c and HbA0 materials, and submit these for listing in the JCTLM database.

No submission has yet been received.

9) JCTLM Secretariat to update database information for the Instand(2006) reference measurement method to indicate to the user that this is a method used by the IFCC

laboratory network, following confirmation from IFCC on whether it should now be designated as an 'IFCC method'.
This issue was dealt with during the meeting, and would be followed up by the action A/12-15.

New Actions:
Action (A/12-16): Secretariat to modify the draft for the updated list of HbA1c measurement methods to merge the Instand database entry with the IFCC HPLC/MS-ESI method which would include the reference Kaiser P. et al. Modification of the IFCC reference measurement procedure for determination of HbA1c by HPLC-ESI-MS, *GMS Ger. Med. Sci.*, 2006, Doc. 06, and to circulate it for comment to C. Weycamp, H. Shimmel, G. Beastall, and P. Kaiser.

Action (A/12-17): BIPM to contact ReCCS to request the complementary information and the submission file for review by JCTLM review team for Proteins.

4.3 Outcomes of the JCTLM and IVD Industry meeting

Dr Beastall reported that a successful JCTLM and IVD Industry meeting on "Meeting Traceability Requirements for IVD Industry" had been held in July, just prior to the AACC meetings. He commented that future meetings would have to be scheduled during the AACC sessions to reach a larger number of IVD industry representatives, and to publicize more widely JCTLM activities.

5. JCTLM WG1

5.1 Approval of Cycle 9 RM and RMP nominations and outstanding issues from previous Cycles

Dr Maniguet presented the nominations for reference materials and measurement methods with the final review teams' recommendations which had been submitted for review to WG1. There were forty-two nominations for reference materials for five groups of analytes, and two nominations for reference measurement methods for two groups of analytes which had been submitted for review cycle 9.

The review teams' recommendations for approval and publication in the JCTLM Database are summarized in the following sub-sections for each group of analytes.

5.1.1 Drugs (Cycle 9) [JCTLM-EXEC/12-26]

There were three nominations for reference materials for Drugs. All of these had been reviewed, and were being recommended for approval and publication in the JCTLM database. In addition, the review team had provided suggestions for improvements in the review reports for two of the pure material CRMs..

It was noted that the review team had made a recommendation for listing the certified reference material for tacrolimus in blood, and it was noted future nominations for reference measurement methods as well as the pure primary calibrator would be useful.

The Committee commented that its members would complete the review of these recommendations by the 15th of January 2013.

5.1.2 Non-electrolyte metals (Cycle 9) [JCTLM-EXEC/12-25]

There were seventeen nominations for two certified reference materials for Non-electrolyte metals. All of these had been reviewed, and were being recommended for approval and publication in the JCTLM database.

5.1.3 Non-peptide hormones (Cycle 9) [JCTLM-EXEC/12-17, 18]

There were three nominations for reference materials, and one nomination for a reference measurement method for Non Peptide Hormones. All of these had been reviewed, of these two reference materials and the measurement method were being recommended for approval and publication in the JCTLM database.

It was noted that the review team members had not reached a consensus for the certified reference material for cortisol in human serum, but had concluded that in line with the quality manual the nomination should be deferred until the producer of the material provide data on the comparison of material with the already listed CRM from another producer.

There was one nomination for a certified reference material for pure cortisol which was listed in the database, and had been re-submitted for review against ISO 15194:2009. The recommendation was to keep the material in the list of higher order reference materials.

5.1.4 Metabolites and substrates (Cycle 9) [JCTLM-EXEC/12-20, 21, 22]

There were fourteen nominations for reference materials, and one nomination for a reference measurement method for Metabolites and Substrates. All of these had been reviewed, and twelve reference materials as well as the measurement method were being recommended for approval and publication in the JCTLM database.

Six of these materials were pure material CRMs of high purity, for which the stated uncertainty had not been truncated to avoid an uncertainty statement which broke the physical limit for purity. Uncertainty statements related to pure material CRMs had been discussed in the July JCTLM WG meetings (JCTLM-EXEC/12-03), and it had been concluded that stated uncertainties should be recalculated so as not to have the upper limit for the range of certified value above 100%. It was further recommended by the WG that the listing of such materials be deferred until the uncertainty was corrected including asymmetric uncertainties, and that the issue be addressed at the CCQM.

The Executive agreed to support the recommendation of the review team and approve the publication of the materials, until an international recommendation was developed on the treatment of uncertainties at the physical limit for purity, which required the truncation of uncertainties in such cases. Consequently, the Executive agreed to approve the two pure amino acid certified reference material nominations that had been deferred from the WG1 Cycle 8 round of nominations.

5.1.5 Proteins (Cycle 9) [JCTLM-EXEC/12-31]

There were four nominations for reference materials for Proteins. All of these had been reviewed, and were being recommended for approval and publication in the JCTLM database. The review team raised the issue that one nominated material had an expiration date of 3/31/2013, and would probably have to be delisted soon after being listed unless the expiration date was extended.

5.1.6 Blood Cell Counting (Cycle 3) [JCTLM-EXEC/12-11, 12]

The Committee had decided during its 9th meeting to defer its decision on the listing of the Erythrocyte and Thrombocyte method nomination in the JCTLM Database until after the submission of the English version of the standards describing the measurement method. The review team leader had indicated in an email that DIN 58932-1, English version was the only required document in order for C3RMMP34-35 (Thrombocyte) to be listed in the JCTLM database, and DIN 58932-3, English version would be needed for C3RMMP31 (Erythrocyte) to be listed in addition to DIN 58932-1.

The review team leader for Blood cell counting had provided the JCTLM with the English version of the DIN 58932-1 [JCTLM-EXEC/12-12], and the publication on Blood Cell Concentration (J. Lab Med 2012; 36(1):25-35) [JCTLM-EXEC/12-12].

The committee commented that its members would review further these recommendations, as well as the documents supporting them to see if the major non-compliances have all been corrected for the outstanding nominations for Blood cell counting by the 15th of January 2013.

Actions

Action (A/12-18): Executive Committee to send their comments on the RT recommendations by the 15 January 2013

5.2 Delisting of RMs and RMPs

There had been one reference material placed on the pdf file for no longer listed reference materials for the reason that it was no longer available.

The committee reviewed and approved the WGs recommendation to remove from the database the Total Protein measurement method which was no longer maintained by CLSI, and to place it in the file for no longer listed methods with a reference to the paragraph 3 and Doumas' references 1 and 2 cited in NRSCL RS5-A2.

Action (A/12-19): JCTLM Secretariat to place the total protein measurement method in the file for no longer listed method with a reference to the paragraph 3 and Doumas' references 1 and 2 cited in NRSCL RS5-A2.

5.3 Progress / plans for Cycle XIII call for RMs and RMPs

Dr Wielgosz confirmed that the new call for nominations for Reference Materials, and Methods would be launched on the 15th of February 2013, with a deadline for submissions in May 2012.

5.4 WG1 quality/ procedure manual

There had been no requests for modifications/updates to the WG1 Quality Manual since the 10th Executive Committee meeting.

5.5 Update on AACC Harmonization Initiative

Dr Beastall reported on the progress on harmonization activities since the 10th Executive Committee meeting, notably the meeting of the WGs in the Harmonization initiative in May 2012 in Washington DC that was attended by Dr Wielgosz as the JCTLM representative. He added that the AACC was funding the Secretariat of the Harmonization Initiative.

During the discussion that followed the Committee strongly supported that JCTLM continues to be involved in the harmonization initiative.

6. JCTLM WG 2 – Reference Measurement Laboratories

Prof Siekmann reminded the members of the Committee of the benefits of linking calibration reference laboratory measurements to measurements made by National Metrology Institutes. The Committee commented that this could be most easily tackled if RELA samples/participation become a permanent agenda item for future CCQM OAWG meetings.

6.1 Update on status of accreditation of Reference Measurement Service Providers

This issue was dealt with under agenda point 3.6.

6.2 Approval of Cycle 7 Laboratory RMS nominations

Dr Maniguet presented the nominations for reference measurement services, which had been submitted for review as part of WG2 review cycle 7. There were five nominations for services for two groups of analyte.

The review teams' recommendations for approval and publication in the JCTLM Database are summarized in the following sub-sections for each group of analytes.

6.2.1 Drugs [JCTLM-EXEC/12-32]

There was one nomination for a theophylline reference measurement service. It had been reviewed, and was being recommended for approval and publication in the JCTLM database.

6.2.2 Metabolites and substrates [JCTLM-EXEC/12-23]

There were four nominations for reference measurement services submitted by two reference laboratories. All of these had been reviewed, and were being recommended for approval and publication in the JCTLM database.

It was noted that there were submissions from a national metrology institute which was accredited against ISO 15195 and ISO/IEC 17025.

6.2.3 Non-Peptide Hormones [JCTLM-EXEC/12-19]

There was one nomination submitted for the revision of a reference measurement service for Cortisol in serum. It had been reviewed, and was not recommended for approval and publication in the JCTLM database. The review team had commented that the laboratory was in the process of getting accreditation as of December 2012, and there were major changes in the measurement principle used that would require the publication of the new method and its re-submission for review to WG1 prior to update the measurement service.

The Committee would review these recommendations by the 15th of January 2013.

6.2.4 Accreditation deadline and actions

The accreditation status of laboratories was discussed under 3.6.

6.2.5 Update on IFCC EQAS results

Prof. Siekmann reminded the Committee that there had been no requests for Vitamins RELA Scheme after this issue was raised last year, but that they were prepared to offer the service if necessary. He pointed out that a new facility was developed for the RELA website to draw the

limit of acceptance of RELA results in the case where the results from five laboratories listed in the JCTLM database were shown.
He reported that the establishment of a blood cell counting trial for calibration laboratories was foreseen, and that a discussion had started on the way to deliver the samples. This work would be made in collaboration with the PTB which had developed the method for such measurements, and this gave the target value for the EQAS scheme for routine laboratories.

6.2.6 Re-review of database entries –post accreditation deadline (2012) and with modified ILC participation requirements

Prof Siekmann reported that the results for the RELA Scheme carried out in 2012 would be available in May 2013. He proposed to review the participation record of the reference laboratories having their services listed in the database in June 2013, and this would include a verification on whether or not they had withdrawn their results following participation in the RELA studies in 2010, 2011 and 2012. The Committee agreed with the proposal and requested that the laboratories would be reminded that they would have to participate in future RELA type Schemes to maintain the listing of their services in the JCTLM Database.

Action (A/12-20): Prof Siekmann to review in June 2013 JCTLM listed reference measurement service providers for compliance with JCTLM requirements for participation in RELA type intra-laboratory comparisons. The information will be provided to the JCTLM Secretariat for a review of the laboratories accreditation status and their participation record in laboratory comparisons as required by the JCTLM rules for listing.

6.3 Progress / plans for Cycle VIII call for Laboratory RMSs

Dr Wielgosz confirmed that the new call for nominations for Reference Measurement Services would be launched in February 2013 in parallel to the call for Reference Materials and Methods.

6.4 WG2 quality/ procedure manual

There had been no requests for update to the WG2 procedure manual after the 10th Executive meeting.

7. JCTLM WG3 - Publications [JCTLM-EXEC/12-10, 29, 30]

7.1 Update on activities

Dr Jones presented the document JCTLM-EXEC/12-30 which included the final draft for the position paper on the history and function of the JCTLM. The Committee agreed with the version with the assumption that the editorial corrections discussed during the meeting would be made, and requested Dr Jones to submit this paper for publication in the CCLM Journal.

Dr Jones introduced the paper JCTLM EXEC/12-29 which contained the draft for the traceability statements for IVD providers' use. In the discussion that followed, the Committee concluded that the JCTLM Secreatrait would comment on version and circulate it for comment to the members of the EC. It was agreed that the finalized statement would ultimately be widely distributed on the Website of the JCTLM, IFCC, and to IVD industry.

Action
Action (A/12-21): Dr Jones to submit the paper the history and function of the JCTLM for publication in the CCLM Journal.

Action (A/12-22): JCTLM Secretariat to comments on the text of the traceability statement and circulate it for comment to the members of the EC.

8. Documents submitted by JCTLM Members and Stakeholders for consideration by the Executive Committee

There were no documents submitted during the year.

9. Liaison with ISO TC 212 [JCTLM-EXEC/12-15, 16]

9.1 Revision of ISO 17511:2003 [JCTLM-EXEC/12-14]

Dr Wielgosz introduced the documents JCTLM-EXEC/12-15, and 16 which included the minutes of the last ISO TC 212 WG2 meeting held in Berlin in August 2012, and the agenda for the next meeting to be held in January 2013.
He pointed out that a drafting team had been appointed for a major revision of the ISO 17511, and it was foreseen that at least three more meetings would be required to update the document. It had been decided that the document would be extend to cover the traceability of measurements on patient samples and that this would be consistent with the new proposed wording of the EU IVD Regulations.

9.2 Revision of ISO 15195

Prof Siekmann reported that the ISO 15195 was being reviewed, including for the consistency of terminology with the VIM3. He added that ISO TC 212 WG2 has agreed with the proposal to include ISO 17025 as normative reference in ISO 15195, which would facilitate the accreditation of reference measurement laboratories.

9.3 Other work items in ISO TC 212

ISO TC 212WG2 had reviewed the ISO/REMCO N1177, *Explanatory Note on Commutability*. The working group concluded that the ISO REMCO document did not adequately or correctly cover the importance of the issue of the commutability of reference materials, and that this was an extremely important issue that impacted upon a broad range of clinical laboratory measurement procedures. These comments had been submitted to ISO REMCO by the end of September 2012.

10. Liaison with the EC

10.1 Update on revision to the IVD Directive [JCTLM-EXEC/12-13]

Dr Schimmel reported that a revised version of the EC Directive on IVD medical devices had been completed, it was now proposed as an EU Regulation, and was tabled for discussion by the European Parliament. The regulation could be voted into force by the end of 2013 with a three year transition period foreseen.
He pointed out that the comments made on metrological traceability by JCTLM and also supported by IRMM had been considered by the European commission, and had been included in the text of the proposed regulation.

10.2 Liaison with the Global Harmonization Task Force (GHTF)

It was noted that the GHTF has become the IMDRF (International Medical Diagnostic Regulation Forum).

11. Liaison with the WHO

11.1 Issues arising from the WHO-ECBS meeting (IFCC)

Dr Beastall informed the committee that the next WHO-ECBS meeting was scheduled in January 2013.

12. Report from related activities/meetings

There were no reports on related activities/meetings.

13. Publicity for the JCTLM

The Committee agreed that a newsletter should be sent be email to the members of the JCTLM to reflect the latest update of the JCTLM database, and publication, as well as to announce the future Workshop & Stakeholder meetings.

Action (A/12-23): Secretariat to send an email to JCTLM members by end of March 2013 on the latest updates for JCTLM activities.

14. Future meetings of the JCTLM

14.1 Meetings for 2013

The 12th meeting of the JCTLM Executive would be held at the BIPM on 27 and 28 November 2013, and the 13th meeting on the 4th and 5th December 2014.

14.2 JCTLM Symposium and Stakeholder meetings for 2013

It was agreed that a Technical Workshop would be held at the BIPM on 25 November 2013 with a morning session on Commutability, and on the impact of changes in reference measurement systems on Clinical Evidence in the afternoon. It would be followed by a Stakeholder meeting on 26 November 2013 on the future and new structure of JCTLM.

15. Close

The Chairman closed the meeting on 7 December at 13:30.

S. Maniguet (BIPM/JCTLM Secretariat)
15/02/13

Revised 19/03/13

Annex 1: Summary List of Actions

Actions from the 11th Executive Meeting

Action (A/12-01): BIPM to contact the Chair of the CCQM OAWG in order to verify the possibility to address the issue of the use of RELA samples for relevant CCQM comparisons as a permanent item agenda future OAWG meetings.
Action (A/12-02): BIPM/NIST to review the information available in the NIST SRM certificates of analysis, and to draft guidance on the correction factors that CRM user would need to apply for the conversion of mass fraction to concentration values for discussion at the next WG meeting
Action (A/12-03): JCTLM Secretariat to liaise with CDC to inform them on the need to clarify to the database user if there were differences in the measurement results obtained in using Abel-Kendall or their improved IDMS method, and to verify the feasibility of a comparative study including patients' sample and spiked steroid samples.
Action (A/12-04): JCTLM Secretariat to write to UME to confirm the Executive's approval of membership.
Action (A/12-05): Dr Schimmel to contact Dr Bei to clarify if she would continue to contribute to the Non-peptide Hormones review team activity, and to confirm if she would be eligible as Leader of the Metabolites and Substrates review team
Action (A/12-06): Secretariat to update the list of review team leaders and members, and to contact new review team leaders informing them of their approved nominations
Action (A/12-07): WG1 and WG2 Chairs/Secretariat to contact the Blood gases experts of the review team to verify the current status of higher metrological order items for Blood gases reference measurement systems.
Action (A/12-08): WG1 Chair/Dr Schimmel to contact Dr C. Jackson to correct the pending issue for the traceability statements and to finalize the nucleic acid review team terms of reference, and to circulate the final version for approval by the Executive Committee.
Action (A/12-09): Dr Schimmel, Dr Beastall, Dr Wielgosz, Dr Jones to draft a paper for next JCTLM Executive Meeting on the future structure, funding, and impact of JCTLM
Action (A/12-10): JCTLM Secretariat to liaise with network laboratories with regards to the accreditation issue of the laboratories participating in the Network
Action (A/12-11): ILAC to contact Accreditation Bodies to confirm whether or not they are able to offer an accreditation service to ISO 15195, for updating the list on the JCTLM website
Action (A/12-12): BIPM to contact the board of Metrologia to see if it would be possible to expand their electronic service to the publication of reference measurement methods in support of the metrological traceability for laboratory medicine community.
Action (A/12-13): JCTLM Secretariat to modify the JCTLM procedures to include the deadline of the 30th of September by which an organization would have to submit the final version in a non-changeable format of the supporting documentation in order to complete the nomination that would have been submitted by the 30th of May of the same year.
Action (A/12-14): JCTLM Secretariat to draft a statement on the differences between both versions of the ISO 15194 standard, and indicate that for reference materials reviewed against ISO 15194:2002, verification of the CRM certificate was required to determine the compliance of the CRM with ISO Guide 34 requirements and the consistency between the commutability statement and the intend use stated in the certificate of the CRM .
Action (A/12-15): JCTLM Secretariat and Dr Jones to review the document with Dr Jackson and circulate the new version to the members of the Executive Committee for comment.

Action (A/12-16): Secretariat to modify the draft for the updated list of HbA1c measurement methods to merge the Instand database entry with the IFCC HPLC/MS-ESI method which would include the reference Kaiser P. et al. Modification of the IFCC reference measurement procedure for determination of HbA1c by HPLC-ESI-MS, *GMS Ger. Med. Sci.*, 2006, Doc. 06, **a**nd to circulate it for comment to C. Weycamp, H. Shimmel, G. Beastall, and P. Kaiser.
Action (A/12-17): BIPM to contact ReCCS to request the complementary information and the submission file for review by JCTLM review team for Proteins
Action (A/12-18): Executive Committee to send their comments on the RT recommendations by the 15 January 2013
Action (A/12-19): JCTLM Secretariat to place the total protein measurement method in the file for no longer listed method with a reference to the paragraph 3 and Doumas' references 1 and 2 cited in NRSCL RS5-A2.
Action (A/12-20): Prof Siekmann to review in June 2013 JCTLM listed reference measurement service providers for compliance with JCTLM requirements for participation in RELA type intra-laboratory comparisons. The information will be provided to the JCTLM Secretariat for a review of the laboratories accreditation status and their participation record in laboratory comparisons as required by the JCTLM rules for listing.
Action (A/12-21): Dr Jones to submit the paper the history and function of the JCTLM for publication in the CCLM Journal.
Action (A/12-22): JCTLM Secretariat to comments on the text of the traceability statement and circulate it for comment to the members of the EC
Action (A/12-23): Secretariat to send an email to JCTLM members by end of March2013 on the latest updates for JCTLM activities.