

SCIENTIFIC DIVISION

61st MEETING
Milan, Italy (May 25 and 26, 2018)

MINUTES (FINAL)

Members:	Abbr.	Term and Time of Office	
Philippe GILLERY (FR) (Chair)	PG	1 st	2017 01 - 2019 12
Christa COBBAERT (NL) (Vice-Chair)	CC	1 st	2017 01 - 2019 12
Joseph PASSARELLI (US) (Secretary)	JP	2 nd	2018 01 - 2020 12
Konstantinos MAKRIS (GR)	KM	1 st	2017 01 - 2019 12
Mario PLEBANI (IT)	MP	1 st	2017 01 - 2019 12
James PIERSON-PERRY (US) (Corporate Rep.)	JPP	2 nd	2018 01 - 2020 12
Karen PHINNEY (NIST Representative)	KP	Consultant	
Heinz SCHIMMEL (JRC Observer)	HS	Observer	
Gary MYERS (US) (Chair JCTLM)	GLM	Consultant	
Chris BURNS (UK) (NIBSC Representative)	CB	Consultant	
Greg MILLER (US) (ICHCLR Representative)	GM	Consultant	
Youchun WANG (CN) (NIFDC Representative)	YW	Observer	

EXECUTIVE SUMMARY - SCIENTIFIC DIVISION 61st MEETING, Milan, Italy, May 25 – 26, 2018.

Present: Philippe Gillery (Chair), Christa Cobbaert (vice Chair), Joe Passarelli (Secretary), Konstantinos Makris, Mario Plebani, (Members), Jim Pierson-Perry (Corporate Representative), Karen Phinney (NIST Representative), Heinz Schimmel (JRC Observer), Gary Myers (SD Consultant/ChairJCTLM), Chris Burns (NIBSC Representative), and Greg Miller (ICHCLR Representative) were in attendance. Apologies received from Youchun Wang (NIFDC Representative).

5.4 EUROPEAN FEDERATION of CLINICAL CHEMISTRY and LABORATORY MEDICINE (EFLM):

The EFLM Science Committee and SD leadership once again agreed there should be close liaison and communication between the two groups. Professor Eric Kilpatrick is the EFLM SC chair. The Science Committee is responsible for scientific matters within EFLM and projects which further the scientific development of EFLM. Activities of the Committee particularly focus on promotion of research that translates the scientific results of clinical chemistry and laboratory medicine to clinical applications and improves patient outcomes through the appropriate use and interpretation of laboratory data in clinical practice. Within the EFLM SC there are working groups on cardiac biomarkers, biological variation, test evaluation, personalized laboratory medicine and a number of others but the general consensus of the SD is that these activities do not overlap with the IFCC SD. Approaches to avoid overlap and work collaboratively are being discussed and explored.

6.1 WORLD HEALTH ORGANIZATION (WHO):

The WHO meeting occurs each autumn. PG attends and participates as the liaison from the SD. The next meeting is in November in Geneva. PG is not aware of any new projects relevant to the SD to consider at this time. CB is now a full member of the WHO Expert Committee (first year) and will be able to provide a complete update from the WHO. The WHO has a different perspective with respect to metrology and as a result, commutability of some of the reference materials needs to be carefully considered. Having CB on the committee will also be helpful to this issue.

6.2 CLINICAL AND LABORATORY STANDARDS INSTITUTE (CLSI):

The complete list of cooperative IFCC/CLSI joint projects is available on the IFCC website. The link to these projects is under CPD: [http://www.ifcc.org/ifcc-communications-publications-division-\(cpd\)/ifcc-publications/clsi-ifcc-joint-projects/](http://www.ifcc.org/ifcc-communications-publications-division-(cpd)/ifcc-publications/clsi-ifcc-joint-projects/).

Jim Pierson-Perry is a member of the CLSI Board of Directors and serves as the IFCC liaison to CLSI and the CLSI liaison back to the IFCC Executive Board. Updates to the key guidance documents for interference testing (EP07-A3 and EP37) were released in April. There are a number of core and relevant documents that are scheduled to be released next year (EP06, 12, 34, and 25).

GM received the Russell J. Eilers Memorial Award (selected by the CLSI President) - CLSI's highest award. This is a significant achievement.

6.22.1 Joint Committee on Traceability in Laboratory Medicine (JCTLM):

The SD encourages visiting the JCTLM website (www.jctlm.org) which provides useful resources to illustrate the importance of traceability in laboratory medicine. The website is targeted at non-specialists and is intended to underpin the new JCTLM tag line 'Accurate results for patient care'. Sections include: Latest News, Publications, Resources, Meetings, and Partners.

The JCTLM 2018 nomination cycle for certified reference materials, reference measurement procedures and calibration laboratories that provide reference measurement services for laboratory medicine and clinical chemistry closed May 30, 2018. As of March 2018, the JCTLM Database contains:

- 296 available certified reference materials;
- 194 reference measurement methods or procedures
- 176 reference measurement services delivered by 17 reference laboratories.

JCTLM and ICSH leadership convened a joint meeting 14-15 May, 2018 at BIPM, Sèvres to discuss technical issues related to reference measurement system traceability for blood cell counting and total hemoglobin. Representatives from ICSH and from PTB, Germany shared their respective approaches to standardization.

6.22.2 Joint Committee for Guide in Metrology (JCGM):

Report from Working Group 1 (GUM - Expression of Uncertainty in Measurement)

There was no new information made available since the last update/meeting minutes published.

Report from Working Group 2 (VIM)

Joint Committee for Guides in Metrology Working Group 2: Professor Ian Young is representing the IFCC on this group. WG2 meets twice per year and each meeting is one week in duration. IY cannot easily commit to attend two one week meetings per year, especially given the content of the meetings and since he is President of ACB. The SD discussed the importance of having IFCC representation in this group and is considering a potential successor for Prof. Young.

6.22.3 BUREAU INTERNATIONAL DES POIDS ET MESURES (BIPM) Consultative Committees

6.22.3.1 Consultative Committee for Amount of Substance: Metrology in Chemistry and Biology (CCQM): PG has been added in JCGM listing (covers CCQM and CCU activities). An invitation was extended to IFCC to attend the CCQM plenary meeting. One agenda topic dealt with reports from international organizations in liaison with the CCQM including the IFCC. Learning more about the standardization activities of the IFCC Scientific Division would be of great interest to the NIM community in the CCQM.

6.22.3.2 CC for Units (CCU): SD received no correspondence.

6.31 JOINT RESEARCH CENTER (JRC) – formerly the INSTITUTE FOR REFERENCE MATERIALS AND MEASUREMENTS (IRMM):

The status of JRC reference materials activity is mostly covered under the respective Cs and WGs. The JRC continues to collaborate with numerous SD Cs/WGs on a variety of projects. Reference materials are still a key area of focus of the JRC

6.33 NATIONAL INSTITUTE OF BIOLOGICAL STANDARDS AND CONTROL (NIBSC)

C. Burns provided the following update:

Three new standards are being proposed - Standards for establishment by WHO:

- Proposed WHO 2nd IS Factor V, Plasma (16/374)
- Proposed 1st WHO RR for CD4
- 2nd International Standards for Prostate Specific Antigen (free) and Prostate Specific Antigen (90:10)

Proposed new standards projects to be endorsed by WHO (5 in total):

- Proposed replacement IS for Ferritin
- The proposed WHO 1st international standards for (Genomic Variants) ctDNA
- Proposed 1st WHO IS for anti-TPO antibodies:
- 2nd WHO IS for Insulin-like Growth Factor-1, recombinant, human, for immunoassay
- Proposed 1st WHO International Genomic Reference Panel for Microsatellite Instability

6.37 NATIONAL INSTITUTE FOR STANDARDS AND TECHNOLOGY (NIST):

The status of NIST reference materials activity is mostly covered under the respective C's and WGs.

In addition, the NIST website (www.nist.gov) can provide information on materials and services available today.

The most relevant projects to the IFCC and SD are:

- Renewal of Troponin
- Vitamin D
- Creatinine in urine

8.2 MAIN ACTIVITIES OF COMMITTEES:

8.2.6 C-NOMENCLATURE, PROPERTIES AND UNITS (C-NPU):

As a reminder, in 2014 a formal agreement between IFCC and IUPAC was put in place. Wikipedia presence for the NPU was created 2015 (edited by the chair with input from many NPU members). The Wikipedia entry is a useful introduction:

(https://en.wikipedia.org/wiki/NPU_terminology) and the NPU Website is performing well. Professor Howard Morris has replaced Professor Graham Beall as IFCC representative to the NPU Steering Committee. In addition, Dr. Flatman, outgoing C-NPU chair is also now a member of the Steering Committee.

A new chair (Dr. Karin Toska) was appointed in March to replace the previous chair. A new member (Dr. van der Hagen – NL) was also appointed. Finally, Dr. Scherrer was confirmed for a second term.

The Committee intends to submit in the near future a publication entitled: "Recommendation on measurement units - why and how" in the electronic Journal of the International Federation of Clinical Chemistry and Laboratory Medicine

8.2.11 C-MOLECULAR DIAGNOSTICS (C-MD):

The Committee had outstanding participation at the Durban meeting in conjunction with WorldLab 2017. The committee reviewed the website and has submitted updates for the EQA page. The committee will request a separate webpage called "Expert Laboratories". During the Durban meeting, the requirements for expert laboratories was redefined which will facilitate expanding the geographical range of the expert laboratories. The committee will use Survey Monkey to streamline and facilitate reporting from network laboratories. Several draft documents regarding Alternate Assessment and EQA implementation have been circulated. During the Durban meeting, a specialty focused approach was viewed as being the best approach rather than a generalized approach to AA and EQA.

Standardization/Harmonization efforts: The committee designed and captured data pertaining to the harmonization of the Molecular report. Sixteen laboratories participated. Publications: The committee is formulating a plan with the new membership regarding future publication efforts.

Paper Accepted: Deborah A. Payne, Ph.D.a, Katarina Baluchova, Ph.D.b, Graciela Russomando, Ph.D.c, Parviz Ahmad-Nejadd, Cyril Mamotte, Francois Rousseauf, Ron H. van Schaik g, Kristin M Marrioth, Masato Maekawai, K.C. Allen Chanj, on behalf of the IFCC Committee for Molecular Diagnostics (C-MD) Toward Harmonization of Clinical Molecular Diagnostic Reports: Findings of an International Survey. CCLM Participation with Industry and other committee representatives: The C-MD participated in surveys requested by Helen Parkes from the ISO regarding reference materials organizations.

The EB decided to merge this Committee with the Task Force on Pharmacogenetics beginning in 2019.

8.2.23 C-TRACEABILITY IN LABORATORY MEDICINE (C-TLM):

A new chair is now in place – Dr. Anja Kessler who replaces Professor Lothar Siekmann and was previously the RELA Consultant on the Committee. There is also a new Observer from China.

The committee continues to focus in the following areas

1. IFCC External Quality Assessment for Reference Laboratories
2. Collaboration between RELA and CCQM Key Comparisons
3. HbA1c Network

The deadline for RELA is now past in May and the SD will learn more about this at the next meeting in November. Dr. Kessler would also like to increase the content of RELA and has some ideas to move this forward.

The Committee is planning to meet in Budapest in November in conjunction with the General Conference.

8.2.24 C-REFERENCE INTERVALS AND DECISION LIMITS (C-RIDL):

The committee has been very active in the last months. Two meetings have been held in 2017 - during the EuroMedlab Congress in Athens and also held during the IFCC WorldLab Congress in Durban. At these meetings, the topics/planned publications of the C-RIDL were discussed and decided as below:

Discussed topics;

1. Indirect reference intervals
2. Clinical decision limit
3. Verification, validation and transference of reference intervals

Planned papers:

- a) Indirect reference intervals
- b) The clinical decision limits versus reference intervals
- c) The verification of reference intervals

Article published on behalf of the C-RIDL:

Jones GRD, Haeckel R, Loh TP, Sikaris K, Streichert T, Ozarda Y,; IFCC Committee on Reference Intervals and Decision Limits. Indirect methods for reference interval determination - review and recommendations. Clin Chem Lab Med. 2018 Apr 19. pii: /j/cclm.ahead-of-print/cclm-2018-0073/cclm-2018-0073.xml. doi: 10.1515/cclm-2018-0073. [Epub ahead of print].

The next C-RIDL meeting will be held on November 9, 2018, during the General Conference in Budapest in Hungary, 2018. This meeting will be the opportunity to discuss and decide about the plans/suggested work items and planned publications of the C-RIDL. These are important as it relates to new activities with CLSI for an upcoming update on the guidance document for Reference Ranges (EP28).

8.2.25 C-STANDARDIZATION OF THYROID FUNCTION TESTS (C-STFT):

The EB approved the appointment of Dr. H. Vesper as C-STFT Chair (2018 – 2020) as replacement of Professor L. Thienpont. In addition, three other new members were appointed as others finished their second term and new consultants were identified. The second phase of the stability study of the free T4 standardization and TSH harmonization panels is on-going and will be followed-up. A network of FT4 reference laboratories is being established. The first method comparison is planned in spring 2018. Operational procedures for the network including evaluation criteria and certifications are being developed. Based on the experiences collected from the network members, the FT4 RMP might be refined. Once the network of reference laboratories for free T4 is established, new method comparison studies with specific patient groups will be initiated. A plan for coordinating national standardization and harmonization activities with the IFCC C-STFT will be developed. The committee will discuss the development of a formal certification program for FT4 and TSH-assays. Two meetings are planned – in July at the AACC Annual Scientific Meeting & Clinical Lab Expo in Chicago, and in November in conjunction with the IFCC General Conference in Budapest.

8.2.26 C-HARMONIZATION OF AUTOIMMUNE TESTS (C-HAT):

The Committee is quite active. The committee continues to focus on the preparation of reference materials in collaboration with the JRC. There are enough samples for a commutability study using the B2GP1 candidate reference material. Analysis will be done by a variety of ELISA methods. A second commutability study is necessary because of inconsistencies identified during the value assignment process. This candidate reference material is stable and homogeneous. The C continues developing plans for introducing and implementing the reference materials for IgG anti MPO and IgG anti PR3. The committee is facing a similar issue as C-STFT with implementation of harmonized assays systems in that there is the need to work with manufacturers and regulatory agencies worldwide and in particular the FDA. At present IVD manufacturers have to submit a full new 510k dossier after they have re-calibrated their assay, including sometimes very expensive clinical studies. This requires considerable resources (financial, people, time) and is often a barrier to standardization/harmonization. The issue is also very international, as the legislation concerning the approval of assays is different in different countries.

The C is planning its next face-to-face meeting in London July 9, 2018.

8.3 MAIN ACTIVITIES OF WORKING GROUPS:

8.3.35 WG - STANDARDISATION OF HEMOGLOBIN A2 (WG-HbA2):

A joint committee with ICHS (The International Council for Standardization in Hematology) has been formed. The method developed is an HPLC-IDMSMS measurement procedure based on peptide mapping and calibration with recombinant expressed HbA0 and HbA2 standard materials, traced back to SI units. The experimental work for the validation of the candidate reference measurement procedure assessing various target tryptic peptides is nearing completion. In the next weeks the WG will prepare the first paper, mostly focused on the description of the new Reference Measurement Procedure for HbA2. Later on, the WG plans to discuss in detail how to structure the second paper, on the validation of this RMP. This second phase will require also the acquisition of new reagents and additional samples will be needed to fully confirm the validation of the method. Since the reagents are quite expensive and sample acquisition requires effort and funding, the WG will only proceed after a careful planning of the new activities and in consultation with the SD. The SD also encourage the WG to engage the ICSH as much as possible to align activities.

8.3.36 WG - STAND. OF CARBOHYDRATE-DEF. TRANSFERRIN (WG-CDT):

The WG has been very active and has accomplished most of the Terms of References but not complete. The WG will continue for the next 1 – 2 years to finish all activities with a new chair - Dr. Jean Deenmamode. The following is a summary of the current focus / projects of the WG:

- Maintaining an international network of reference laboratories
- Supporting worldwide standardization of commercial methods against the RMP
- Obtaining JCTLM approval for the standards developed by the WG
- Promoting the use in national and international EQAS programs
- Promoting the use of the RMP and the IFCC approved URL and cutoff by national societies involved in alcoholism diagnosis
- Supporting the proper use of CDTIFCC in national guidelines concerning driver checks and workplace checks

To sustain the activities, the WG is looking into identifying new members and to expand the numbers of labs performing the reference methods. Ring Trials are ongoing with the reference laboratories. Manufacturers have agreed to implementation from June – December 2018.

WG-CDT linked articles:

IFCC eNews Nov-Dec 2017 – IFCC standardization of CDT

Research Gate – Statement and DOI (by JW);

https://www.researchgate.net/publication/321979407_IFCC_statement_International_standardization_of_CDT_measurement_leads_to_significant_changes_and_improvements_in_2018.

8.3.39 WG – STAND. OF ALBUMIN ASSAYS IN URINE (WG-SAU):

All activities of the WG-SAU are a joint effort with the Laboratory Working Group (LWG) of the National Kidney Disease Education Program (NKDEP), USA.

The WG-SAU intends to complete data analysis for the urine albumin freeze/thaw study and pursue publication submission in the Summer of 2018.

The WG-SAU intends to issue recommendations for reporting urine albumin and urine protein, in addition to the ACR and PCR, when the measured values are below or above the analytical measurement range for the measurement procedures.

Candidate isotope dilution liquid chromatography tandem mass spectrometry (ID-LC-MS/MS) reference measurement procedures for UA are under development by the Mayo Clinic Renal Function Laboratory and NIST. It is anticipated the NIST procedure will enable assessment of the molecular forms of albumin in urine that may be of importance in the specificity requirements for routine measurement procedures. NIST and Mayo have

performed multiple comparison studies between the two candidate reference measurement procedures. There were some unexplained discrepancies that are under investigation.

Reference materials for UA and urine creatinine:

SRM 2925 Human Serum Albumin from NIST is a primary certified reference material for use with higher order reference measurement procedures for albumin. The material is not yet available on the NIST website. Expected to come out at the end of 2018.

To facilitate standardization of routine methods, NIST SRM 3666 is currently being developed based on the specifications recommended by the WG-SAU and the LWG of the NKDEP. Progress is being made but there is still more to do before this is externally available.

A joint meeting of the WG-SAU and LWG of NKDEP will be held on August 1st, 2018 during the AACC annual meeting.

8.3.40 WG – STAND. OF PREGNANCY-ASS. P-PROTEIN A (WG-PAPPA):

The goal of PAPP-A standardization phase 3 is to study whether pooled 3rd trimester or 2nd trimester serum can be used for harmonization of the commercial PAPP-A tests.

To evaluate whether pregnancy serum derived materials can be used to harmonize the commercial PAPP-A assays aimed for prenatal Down syndrome screening, samples were prepared at the University of Turku in December 2017 and sent out to companies around the change of the year. 4/5 companies delivered results as expected, by mid-February. If significant delays continue with this 5th company, the WG will proceed to analyze the results of the 4 companies and will discuss the results in order to draw preliminary conclusions and plan for future activities.

Publication:

A manuscript has been in preparation around the topic of the WG. The chair intends to first assess the results of the latest analysis in order to possibly include this data in the publication.

Membership:

The list of members of the WG was updated at the beginning of this year to include the members that have been active within the group in the past. In addition, the list of company representatives has been updated according to the newly established collaborations during last year. The status of PerkinElmer (the 5th company) remains unresolved.

8.3.41 WG – GROWTH HORMONE (WG-GH)

The composition of members, terms of reference and current projects have now been identified and can be found on the IFCC website. There is still a need for the inclusion of at least one more reference laboratory. The key term of reference is to achieve standardization of growth hormone through secondary reference materials and a reference measurement procedure by:

- defining the analyte/measurand to be measured
- testing the feasibility of serum pools as secondary, commutable reference preparations
- preparation of secondary reference preparation for GH (3 serum pools)
- development of a LC/MS/MS based reference method for GH

The group has made some progress in trying to develop secondary calibrators that are commutable. It is the intention to do comparison studies between the LC/MS reference method and commercial methods. Preliminary studies have taken place and results indicate that commutability is quite good at low levels but not at the high concentrations. Further studies are planned. The SD also plans to contact LGC which may have developed a method for GH. The inclusion of a term of reference for IGF-1

standardization is still being considered by the WG and the SD. This will be further defined in the coming months.

8.3.42 WG – STANDARDIZATION OF INSULIN ASSAYS (WG-SIA)

This is a joint project between ADA/EASD and IFCC. The overall goal of the WG is to establish a reference system for serum/plasma insulin measurement to achieve standardization of all commercial methods to assay insulin.

The intent is to use the WHO material to calibrate the mass spectrometry method and then to do value assignment of the pools.

Planned activities include:

1. Continued validation of an appropriate intact insulin assay via LC-MS/MS that meets all analytical and clinical specifications for insulin testing.
2. Continue collaboration with Dr. Chris Burns and colleagues at NIBSC to evaluate and assist with validation of new recombinant insulin candidate reference material.
3. Establish serum pools for insulin (and C-peptide) proficiency testing via College of American Pathologists to assess the comparability of results across assays, using a commutable matrix, and to move towards standardization.
4. Peer-reviewed publications regarding either insulin/C-peptide serum pool data across hundreds of laboratories/assays and/or lack of harmonized conversion factor across insulin assays.

8.3.43 WG – STANDARDIZATION OF TROPONIN I (WG-TNI)

The WG has been quite active in the last months. The draft protocol for recruitment of subjects with elevated cardiac troponin I due to acute myocardial infarction and collection of samples for use in comprising SRM 2922 was circulated to all members of the WG TNI. This protocol was finalized by Drs. Christenson and Lowenthal and has been submitted to the University of Maryland Baltimore Institutional Review Board (IRB). This protocol is currently going through the IRB examination procedure; the WG should have feedback beginning of June. Following IRB approval, collection of samples will be initiated. The progress of this collection will be communicated to all engaged with the WG-TNI Standardization program. A meeting of members and others engaged in the WG-TNI Standardization activities will be held at the AACC Annual Meeting in Chicago in August. In addition to this meeting, several members of the WG-TNI confirmed that they will attend the IFCC General Conference this coming November in Budapest. Corresponding members as well as corporate members will also be invited and their participation welcomed. This meeting will be conducted on Friday, 9 Nov 2018, from 13.00-17.00 in a meeting room to be defined.

8.3.48 WG – PARATHYROID HORMONE (WG-PTH):

Good progress is being made with the mass spectrometry PTH method being developed by Dr. Hubert Vesper's group at CDC. A protocol is being finalized for experimental work to compare recognition of PTH by immunoassay with available mass spectrometry methods including that at CDC. Specimens will be distributed in June in order to have results available before the AACC meeting. Work of the IFCC Working Group will be presented in a scientific symposium entitled "Towards improving parathyroid hormone measurements and management of the CKD-MBD" at the AACC in Chicago. [Thursday 2nd August, 10:30-12:00]. An informal meeting of the PTH Working Group is planned for the AACC meeting. A further meeting of the Working Group will be held at the IFCC General Conference in Budapest.

WG-PTH will close in January 2019 and activities resumed under a new Committee on Bone Metabolism to be formed to consolidate WG-PTH, WG-SBMA, and WG-Vitamin D standardization.

8.3.49 WG – CSF Proteins (WG-CSF):

The WG is in contact with NIMs for the standardization of the Tau proteins. There seems to be some coordinated activities.

Three reference materials have now been produced for A β 42, with high, middle and low A β 42 concentration. Homogeneity and stability have been verified, long-term stability (1 year) is acceptable. Value assignment is on-going, with four LC-MS datasets received and being analyzed. A β 1-42 CRM is almost complete and will become available soon. The WG is also developing a SRM mass-spec method for A β 1-42 in CSF, to qualify as a reference measurement procedure (RMP). The WG will continue to refine these materials and procedures as well as for A β 40 which is gaining interest clinically. In addition, activities continue on the tau RMP.

Some manufacturers are having issues with A β 1-42 and the issues may have been underestimated. Apparently it is quite sticky to just about everything.

8.3.50 WG – Standardization of Bone Marker Assays (WG-BMA):

This is a joint activity with the International Osteoporosis Foundation (IOF). The National Bone Health Alliance (NBHA) also has a WG focused on bone marker standardization. All three organizations will be working collaboratively on this project. The American Society of Bone and Mineral Research (ASBMR) also have a WG, but not sure if ASBMR will join with other groups.

The comparability study of the two major clinical assays for CTX and PINP have been completed at four European centres including data on the effects of serum or plasma specimen, fasting or non-fasting subjects and males and females presenting to osteoporosis clinics on the comparability of the results of assays from two manufacturers used by clinical laboratories. Draft manuscripts are being finalized in preparation for submission to an appropriate peer-reviewed journal. Manuscript will also be completed including an algorithm for the harmonization of the results from each assay. For CTX, the likely conclusion is that standardization/harmonization may not be possible unless manufacturers make changes. The situation for P1NP is considerably better and harmonization is likely possible.

The WG will merge with the PTH and vitamin D standardization workgroups in 2019 and will become a Committee. The IOF has agreed that this Committee remains a joint Committee with the Chair: Etienne Cavalier.

The WG would like to focus next on bone alkaline phosphatase standardization.

8.3.51 WG – Commutability (WG-C):

Three papers have been published in Clinical Chemistry:

- W. Greg Miller, Heinz Schimmel, Robert Rej, Neil Greenberg, Ferruccio Ceriotti, Chris Burns, Jeffrey R. Budd, Cas Weykamp, Vincent Delatour, Goran Nilsson, Finlay MacKenzie, Mauro Panteghini, Thomas Keller, Johanna E. Camara, Ingrid Zegers, Hubert W. Vesper, for the IFCC Working Group on Commutability. IFCC working group recommendations for assessing commutability part 1: general experimental design. Clin Chem 2018;64: 447-54.
- Goran Nilsson, Jeffrey R. Budd, Neil Greenberg, Vincent Delatour, Robert Rej, Mauro Panteghini, Ferruccio Ceriotti, Heinz Schimmel, Cas Weykamp, Thomas Keller, Johanna E. Camara, Chris Burns, Hubert W. Vesper, Finlay MacKenzie, W. Greg Miller, for the IFCC Working Group on Commutability. IFCC working group recommendations for assessing commutability part 2: using the difference in bias between a reference material and clinical samples. Clin Chem 2018;64:455-64. This paper includes a worked example as supplemental information.
- Jeffrey R. Budd, Cas Weykamp, Robert Rej, Finlay MacKenzie, Ferruccio Ceriotti, Neil Greenberg, Johanna E. Camara, Heinz Schimmel, Hubert W. Vesper, Thomas Keller, Vincent Delatour, Mauro Panteghini, Chris Burns, W. Greg Miller, for the IFCC Working Group on Commutability. IFCC working group recommendations for

assessing commutability part 3: based on the calibration effectiveness of a reference material. Clin Chem 2018;64:465-74. This paper includes additional example data and statistical tools as supplemental information.

The WG will continue the preparation of three additional manuscripts. The overall goal is to propose standard terminology to describe the degree of commutability of a reference material, taking into account its intended use. In addition, to provide guidance to manufacturers and laboratories about what information should be provided by manufacturers in relation to the commutability of reference materials used to establish the calibration traceability of a measurement procedure.

8.3.53 WG – Immunosuppressive Drug (WG-ID):

The WG-ID was newly formed in January 2018. Establishing the chain of traceability for a TDM application is almost uncharted terrain in laboratory medicine. For immunosuppressive drugs, traceability is not given at all - any of the commercial IVD kits, calibrators, and assays do solely assume comparability by participation in proficiency testing schemes usually made up by control matrices or fortified human matrices. Consequently, lab to lab comparison is challenging on the single patient level; changing back and forth between different assay types, even between different LC-MS/MS developed tests may lead to challenging interpretations.

Within the first year of its operation the WG will establish a regulatory framework (operational layout) for the development of reference procedures and reference materials capable to be JCTLM listed. It is desired to come at least to a scientific community based solution, a network of reference laboratories as exemplified for HbA1C in the recent past, could be one solution. As an alternative the engagement of a national metrological institute operating under ISO 17025 and 15195 is desired but not a must to proceed with the project. This framework will be presented at the Budapest IFCC General Conference in November. A second topic to be targeted in the months to come is the question of the status quo in ID-measurement. It is envisioned to collect and distribute sample sets between a number of selected laboratories of WG members. The minimum requirement will be to send out frozen samples, as everyone is well aware of the quite complicated situation to distribute native whole blood specimen between laboratories.

8.3.54 WG – Apolipoproteins by Mass Spectrometry (WG-APO MS):

The WG is progressing very well and investigating both reference materials and reference methods. The Working Group has been proceeding along two lines:

1. Three calibration labs (CDC/ Atlanta, Leipzig and Leiden) are working on the development of a common, multiplex LCMS method for quantifying serum apolipoproteins. Progress is being made yet it is quite a challenge to develop a method that is suitable for several apo proteins, including Apo(a). The goal is to develop a common method as much as possible. The trypsin digestion step is also being investigated. The next meeting is planned for September.
2. In collaboration with JRC and LNE, the WG is pursuing the development of Reference Materials for LCMS quantitation. Many steps have to be taken and good progress is being made. The WG is first focussed on serum/plasma apo(a) standardization. Special thanks to Prof. Kostner, months of negotiations and effort in purchasing EDTA-plasma with transgenic apo(a) from pigs in Japan. The material arrived on 29 March. In May a mini-telco is planned on how to assess its suitability (commutability) for harmonizing/standardizing apo(a) or Lp(a) assays. A protocol for a commutability study is also in development.

8.3.55 WG – Pancreatic Enzymes (WG-PE):

The WG was established as a result of the closure of the previous C-RSE and initially established the following Terms of Reference:

- To develop a primary reference method for pancreatic Lipase in Serum
- To develop a primary reference method for pancreatic Amylase in Serum
- To support EC-JRC (Joint Research Centre, Directorate F – Health, Consumers and Reference Materials, formerly IRMM) in case of studies and certification of reference materials for enzymes.

The development of reference method for pancreatic lipase in serum is not feasible and as the SD previously decided, activities should stop on this. The new terms of reference will focus on the development of a reference system for pancreatic amylase in serum. For amylase, results so far look quite promising and with acceptable stability. The majority of the work is being directed and performed by the WG chair. The chair intends to contact the former companies of the previous committee to get more involved with future studies and implementation.

As in the past in C-RSE, the WG will continue to support JRC with regard to reference materials of enzymes.

The next meeting of the WG will likely take place sometime in 2018 in conjunction with an international conference.

8.3.56 WG – Fecal Immunochemical Testing (WG-FIT):

Key outcomes as last reported;

- Development of a reference material/ method for FIT: a reference lab in Belgium to collate information via surveying all the FIT companies. This has been carried out and results to be discussed at the next FIT meeting to enable progression.
- Challenges of EQA schemes include the pre-analytical variation of a stool sample being loaded into a collection device so the group has discussed making a formal recommendation that EQA schemes have two parts (1) sample pre-loaded to only assess the performance of the analyzer (2) provide sample to assess whole pathway from sample loading to result. This needs further discussion and ratification at the next meeting.
- A second meeting took place on Thursday 26th October 2017 in Barcelona. This coincides with a World Endoscopy Organization (WEO) meeting where many group members will already be present. Agenda included discussion of the above two topics, clarification of terms of reference of the WG, and how sponsorship funds should be allocated.
- Funding: the group has been successful in obtaining sponsorship from a number of diagnostic companies that have FIT analyzers.

8.3.57 WG – Cell Free DNA and related circulating biomarkers (WG-cfDNA):

The activities of the WG are just starting to get underway. The WG has reached out for corporate member sponsorships to enable face-to-face meetings.

Terms of Reference:

- To identify and provide guidance on preanalytical and analytical aspects for obtaining good and reproducible results for cfDNA and related circulating biomarkers for clinical use, and to guide the correct clinical implementation of these biomarkers.

Current projects:

- Defining pre-analytical aspects / drafting guideline
- Defining minimal analytical performance
- Setting up proficiency testing for cfDNA
- Organizing international workshops
- Defining grant proposals to address unmet needs

8.3.58 WG – Procalcitonin (WG-PCT):

The activities of the WG are just starting to get underway. The following is the status of WG-PCT to date:

Current projects:

- Production of EQA materials that will be used to assess comparability of results provided by the different PCT assays
- Production and characterization of a primary calibrator that will be used to calibrate the candidate reference method
- Development of separation methods to purify PCT in biological samples
- Development of a candidate reference method for absolute quantification of PCT by IDMS

Future Projects:

- Commutability assessment of candidate EQA materials designed to assess comparability of results provided by the different PCT assays
- Evaluation of the analytical performance of a candidate reference method for absolute quantification of PCT by IDMS

8.3.59 WG – Vitamin D Standardization Program (WG-Vit D)

The WG has only been established since the beginning of the year. The group plans to meet at the AACC in Chicago in August. Inputs are needed from all key stakeholders, especially the IVD companies. This is especially true to gather information on reference ranges and how these were determined. This WG has been established in preparation for the new Committee on Bone Metabolism to form in 2019 along with WG-PTH and WG-SBMA. The chair of this new C will be Professor Etienne Cavalier who is the current chair of WG-SBMA. Therefore, this is a year of transition for WG-Vit D.

The WG established the following Terms of Reference for 2018:

- Re-evaluate current Vitamin D Standardization Program (VDSP) performance guidelines for serum total 25-hydroxyvitamin D measurement, i.e. Total CV \leq 10% and Mean Bias \leq 5% (Clin Chim Acta 2009;408:8-13).
- Establish VDSP performance guidelines for 3-epi-25-hydroxyvitamin D and 24,25-dihydroxyvitamin D3.

8.19 MEETINGS

- 8.19.61 61st SD Meeting – Milano, Italy, May 25 – 26, 2018
- 8.19.62 62nd SD Meeting – Budapest, Hungary, November 8 – 9, 2018
(in conjunction with the IFCC General Conference)
- 8.19.63 63rd SD Meeting – Barcelona, Spain, May 18 and 19, 2019
(Saturday and Sunday), before the EuroMedLab Congress.
- 8.19.64 64th SD Meeting – Milano, Italy, October 11-12 and/or 18-19, 2019
(Friday-Saturday) at the IFCC office.