SCIENTIFIC DIVISION

55th MEETING
Paris, France (2015 06 19-20)

MINUTES *(FINAL)*

Members:	Abbr.	Term and Time of Office
Ian YOUNG (UK) (Chair)	IY	2nd 2014 01 - 2016 12
Philippe GILLERY (FR) (Vice-Chair)	PG	2nd 2014 01 - 2016 12
Joseph PASSARELLI (US) (Secretary)	JP	1st 2015 01 - 2017 12
Christa COBBAERT (NL)	CC	2nd 2015 01 - 2017 12
Giampaolo MERLINI (IT)	GMl	2nd 2014 01 - 2016 12
Tsutomu NOBORI (JP)	TN	1st 2015 01 - 2017 12
James PIERSON-PERRY (US) (Corporate Rep.)	JPP	1st 2015 01 - 2017 12
David BUNK (NIST Representative)	DB	Consultant
Heinz SCHIMMEL (IRMM Representative)	HS	Consultant
Gary MYERS (US) (JCTLM Representative)	GLM	Consultant

EXECUTIVE SUMMARY - SCIENTIFIC DIVISION 55th MEETING, PARIS, FRANCE, JUNE 19-20, 2015.

Present: Ian Young (Chair), Philippe Gillery (Vice-Chair), Joe Passarelli (Secretary), Christa Cobbaert, Giampaolo Merlini, Tsutomu Nobori, Jim Pierson-Perry (Corporate Representative), David Bunk (NIST Representative), Heinz Schimmel (IRMM Representative), Gary Myers (JCTLM Representative), were in attendance. Chris Burns from NIBSC, attended Day 2 in the afternoon. Apologies received from Ms Paola Bramati (IFCC Office).

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

The EFLM Scientific Committee and SD leadership once again agreed there should be close liaison and communication between the two groups. Elvar Theodorsson, Linköping University, Sweden, is the Chair of the EFLM Science Committee. IY indicated he has been in communication with Elvar and will continue to provide him with the minutes of SD meetings.

EFLM held a meeting November 24-25, 2014 in Milano, Italy titled, “Defining analytical performance goals 15 years after the Stockholm Conference”. This conference dealt with analytical performance goals and quality requirements of laboratory tests. IY and PG attended the meeting. There could be some overlap considering the global reach of some of the planned activities coming from the meeting. For example, the EFLM has established Task & Finishing Group “Biological Variation Database” with Prof. Sverre Sandberg as chair. CC from the SD has been asked to work in this group. In addition,

corporate members have expressed some concern in the perceived overlap of activities between the IFCC and EFLM.

6.1 WORLD HEALTH ORGANIZATION (WHO):

WHO meetings occur each Fall. PG attends and participates as the liaison from the SD. The SD decided that there were no new projects or collaborations to propose in 2015.

6.2 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/

6.22.1 JCTLM:

The JCTLM Executive is looking to increase the level and recognition and acknowledgement of the JCTLM and the database that it produces. At the December 4-5, 2014 meeting of the JCTLM Executive Committee, the Committee approved the Chairmanship of Dr. Gary Myers and the BIPM's continued role as Secretariat for the JCTLM. In addition, the JCTLM Executive Committee established an ad-hoc Working Group on JCTLM Governance which is tasked to revise JCTLM procedures, and propose the most appropriate organizational structure and assignment of duties. JCTLM Executive Committee created a Working Group on Traceability: Education and Promotion. The aim will be to produce and promote educational materials to demonstrate the value of traceability in laboratory medicine as a means to reduce between method variability in the interests of improved clinical outcomes and patient safety. Dr. Graham Beastall will serve as the new Working Group Chair.

6.22.2 JCGM:

A workshop on Measurement Uncertainty took place on 15th and 16th June 2015, followed by a three day meeting of WG2 (17th-19th June 2015), which allowed for the discussion of significant matters raised during the workshop. In addition, several other meetings are planned in 2015 for both WG1 (GUM) and WG2 (VIM).

Thirty informative annotations have been developed to go beyond the formal Notes and provide more detailed description and definition of terms appearing in VIM 3. It is planned that these annotations will be published on a new BIPM website. Further annotations will be developed, all of which will be incorporated into VIM 4, which is currently being developed by WG2 (VIM).

6.22.3 BIPM Consultative Committees

SD received no correspondence from CCQM or CCU.

6.31 INSTITUTE FOR REFERENCE MATERIALS AND MEASUREMENTS (IRMM):

IRMM continues to collaborate with numerous SD Cs/WGs on a variety of projects.

6.33 NATIONAL INSTITUTE OF BIOLOGICAL STANDARD AND CONTROL (NIBSC)

IY is now a member of the NIBSC Scientific Advisory Committee. IY invited Chris Burns (NIBSC) to provide an overview to the SD on Day 2. NIBSC has been involved in 4 IFCC Working Groups to date.

In addition, Chris Burns (NIBSC) had contacted IY to see if the SD would be interested in forming a WG to prepare new PSA reference material. DB indicated that NIST may be interested in sending a representative to NIBSC meetings who could also attend on behalf of IFCC SD.

IY invited Chris Burns to join the IFCC SD on a formal basis to improve the collaboration with the NIBSC. Chris Burns will discuss this further within the NIBSC organization.

6.37 NATIONAL INSTITUTE FOR STANDARDS AND TECHNOLOGY (NIST):

NIST continues to collaborate with numerous SD Cs/WGs on a variety of projects.

8.2 MAIN ACTIVITIES OF COMMITTEES:

8.2.6 C-NPU:

A new website for the international version of the NPU terminology – sponsored by IFCC is in development. The 2nd edition of GUM (JCGM 100) has now been issued as a draft.

The Silver Book v.2 has been submitted, reviewed, revised and resubmitted for publication. Both an e-version and hard copy book will be created. Once the Silver Book goes online, the C-NPU will assume responsibility for updating when needed. IUPAC will not produce paper editions of the 'Color books' in the future.

8.2.11 C-MD:

A manuscript has been proposed for the special edition of CCA entitled: *"Pre-Examination Factors Affecting Molecular Diagnostic Testing: a Case based approach"*. The International Network of IFCC Centres in Molecular Diagnostics has been renewed. With respect to the website, links to AIMS and Molecular Centers have been reviewed, added to, and harmonized. EQA and PT list has also been added to the site. The committee has expanded into Latin / Central America with Mexico now included.

8.2.21 C-RSE:

The two activities the C-RSE has in place are: 1) evaluation of the commutability of IRMM candidate CRMs for ALT, LDH, and CK and 2) refinement of the pancreatic lipase reference method. Progress on pancreatic lipase standardization has been achieved but there is still more to do. Significant interlaboratory discrepancies are still present. Less progress has been made with respect to the value assignments of the IRMM candidate CRMS. There is a proposal in consideration to close the committee and form a new Working Group specifically on the standardization on pancreatic lipase.

8.2.23 C-TLM:

The C-TLM requested that the SD establish a new working group to address several issues and design a generally accepted reference measurement procedure for the measurement of total protein. This was accepted by both the EB and SD and G. Schumann has submitted a project proposal. IY will ask G. Schumann if he is willing to step down from the C-TLM committee to form this new WG. The SD had concerns with the HbA1c Reference Lab Network with respect to the numerous modifications to the official IFCC Reference Method that now exist. It has now been confirmed that the 2008 modification published in Clinical Chemistry is being used by the laboratories in the network and as indicated in the JCTLM data base. Therefore, this concern has been resolved. The C-TLM also continues to provide an interface between IFCC and the JCTLM Working Groups.

8.2.24 C-RIDL:

The C-RIDL continues to work to establish regional reference intervals. These regional reference intervals should be traceable to reference measurement procedures where possible. Considerable activity has occurred in the Middle East. The C-RIDL plans to meet in Paris in conjunction with 2015 EuroMedLab. An update will be provided at the next SD meeting.

8.2.25 C-STFT:

The technical standardization (FT4) and harmonization (TSH) Phase IV is complete. All measurements (by immunoassays and the ID-MS reference method for FT4) are also complete. Data analysis is on-going and a first report will be presented/discussed in conjunction with the AACC in Atlanta. A total of 11 companies participated in the studies and 300 patient samples with balanced patient groups were tested. The committee is also in discussion with key stakeholders to implement the use of the traceable assays in routine clinical practice as reference intervals will change.

8.3 MAIN ACTIVITIES OF WORKING GROUPS:

8.3.35 WG-HbA2:

The committee plans to meet in Paris in conjunction with 2015 EuroMedLab. The main activities of the WG have been concerned with the development of the reference measurement procedure. Preliminary experiments showed the method to be feasible and reproducible. The committee is also working with IRMM for certified reference materials. A manuscript will be submitted to CCA on a reference method. The SD decided to close

this WG at the end of 2015. The International Council for Standardization in Hematology (ICSH) also has a program to standardize HbA2. A joint ICSH – IFCC group may be formed once WG-SHbA2 is closed.

8.3.36 WG-CDT:

There are now 6 labs in the reference network (4 old and 2 new). The 2 new labs have demonstrated comparable results. A HPLC method has been developed and uncertainty and robustness is being assessed. Decision limits and clinical impact are also being assessed as a second step. The group plans to submit a paper on the method as well as a second paper on guidance on CDT in laboratory practice.

8.3.39 WG-SAU:

All activities of the WG-SAU are a joint effort with the NKDEP Laboratory Working Group. The next meeting of the WG-SAU meeting is planned to be held in conjunction with the 2015 AACC Annual Meeting, Atlanta, GA. The status of harmonization among commercial immunoassays for UA will be discussed. A joint meeting including NKDEP and representatives from each major manufacturer was held on Feb 5th, 2015 at the NIH campus in Bethesda, MD. The goals of the meeting were to discuss the need for improvement of method performance to accomplish standardization and to plan for implementing standardization of the routine methods in the next several years. The next step is to perform a freeze-thaw study to assess the ability to use frozen samples for the commutability study. The status of the reference measurement procedure for UA was also discussed. Laboratory data is being analyzed and compared and NIST and Mayo will collaborate to compare results of their respective candidate reference measurement procedures. Reference materials for UA and urine creatinine were also discussed. IRMM: ERM-DA470k/IFCC Human Serum diluted to concentrations suitable for urine albumin and a candidate secondary urine albumin reference from JSCC (Japanese Society of Clinical Chemistry) were included in the assessment of harmonization to evaluate its commutability and potential to harmonize results for 16 commercial measurement procedures. A commutability study for the NIST Albumin in Human Frozen Urine standard reference material (SRM 3666) will be carried out as a follow-up study. The commutability study will involve a panel of individual urine patient samples and include all/most of the routine clinical methods for albumin in urine.

8.3.40 WG-PAPPA:

The group is essentially just getting off the ground again with a new chair - Sara Wittfooth (FI). The WG-PAPPA previously used purified material to assess ability to standardize assays, but did not work for all assays. The group will assess the potential of harmonization and the goal of making assay results more comparable. Therefore, the group name will be changed to Harmonization.

8.3.42 WG-SIA:

This is a joint project between ADA and IFCC. Establishment of a reference measurement procedure for serum insulin is on-going. Several labs are currently testing samples with the candidate reference method.

8.3.43 WG-TNI:

Currently the WG is developing a CRM for Troponin I in serum and patient samples are being collected at R. Christenson's lab to perform the value assignment. Julian Barth's lab is also collecting additional samples to check commutability. A publication is in preparation and a meeting planned in conjunction with the 2015 AACC in Atlanta. The purpose of this meeting is to bring in manufacturers for value assignment with their respective assays/technologies. Decision limits will change. In addition to this, the AACC will be coordinating the collection of a very large number of samples at the annual meeting. DB also stated that high sensitivity assays are being discussed as well as POC devices in the long term. The Troponin and Natriuretic Peptide tables on the IFCC website will continue to be updated by the WG-TNI.

8.3.45 WG-HAT:
A meeting was held in Brussels Feb 20th 2015 and a meeting planned in conjunction with the 2015 EuroMedlab in Paris. One of the main activities of the group is to produce well-characterised pure antibody preparations with known concentration and identity and use these to transfer values to a matrix preparation. To this end, the report and certificate for ERM DA 476 for IgG anti MPO was released in April 2015 and this material is now available from the IRMM as a Certified Reference Material. A large group of well characterised clinical samples (Prof Xavier Bossuyt) will be analyzed with respect to ERM-DA476/IFCC. Information is in preparation to guide companies on how to transfer values from ERM-DA476/IFCC to their local or kit calibrators and to demonstrate the value of a certified reference preparation. Education is a key activity of the WG, and to offer a consistent and aligned message about ERM-DA476/IFCC and to inform users of how it is best implemented. Discussions with the FDA are currently ongoing and have been informative and supportive of these activities.

8.3.46 WG–cMSP:
A meeting is planned in conjunction with the 2015 EuroMedlab in Paris. Three laboratories were involved in the QA/QC hepcidin assay. They analyzed 5 pools of samples with different hepcidin values. In parallel there is a working group of the French society (SFBC) which also generated pools of samples with different concentrations of hepcidin. The different laboratories participating in the WG have different operating procedures to perform quantitative mass spectrometry analyses for peptides and proteins. These differences are related to the type of analyzers and the type of analytes. Plan for the next WG meeting is to list the different approaches and eventually to prepare a common manuscript on that issue. Several WG IFCC laboratories have available methods to measure apolipoproteins in blood.. As presented by Vincent Delatour there is an ongoing inter-comparison program on ApoB "BioSITrace" coordinated by Helen Parkes. Vincent is leading one of the WP and after discussion the proposition is that IFCC WG-cMSP could contribute to the "BioSITrace" program by analyzing pools of samples.

8.3.48 WG-PTH:
The WG-PTH continues to work on developing a reference system for PTH.

8.3.49 WG–CSFP:
University of Gothenburg, Sweden has collected a large (5 litre) pool of CSF to be the basis for the reference material. A first commutability study has been done, comparing the candidate CRM as well as spiked variants and pools containing detergents. A second commutability study has been performed, in which a common calibrator (Aβ1-42 peptide) was used, and the candidate CRM included. It has been decided that the high-volume samples for the CRM will be pooled based on the original Aβ1-42 levels, so that three different CRMs will be produced with high, medium and low levels. These data are part of a manuscript (under review among co-authors) containing data from both commutability studies.
With respect to the establishment of Reference Measurement Procedures (RMP) for the key measurands (Aβ1-42 and tau) for assignment of values to the reference materials, both Univ. of Gothenburg and Univ. of Pennsylvania have made a full validation, according to ICH guidelines, of their SRM mass spec assays for CSF Aβ1-42. Both labs have also submitted their methods to JCTLM for review.

8.3.50 WG–SBMA:
This is a joint activity with the International Osteoporosis Foundation. 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 it is not certain if ASBMR will join with other groups.

This working group recently met in Milan to look at the preanaytical factors and will be looking for funding which may be requested by the other two organizations that are involved as well.

8.3.51 WG-C:

The WG held a meeting on May 11 via teleconference and plan to hold meetings in conjunction with 2015 EuroMedLab meeting in Paris and at the 2015 AACC meeting in Atlanta. WG-C has also prepared a draft guidance document - *Guide to Assessment of Commutability* which includes sections on definitions, models, experimental designs, discussion of assumptions, interpretation, assessment, verification of commutability, and an extensive statistical analysis tools and methods section.

Greg Miller (chair) and IY have discussed the possibility of combining with ISO and CLSI guidance documents that already exist or as they come up for revision. This will be further discussed to ensure alignment of guidance coming from several organizations.

8.19 MEETINGS

8.19.56 56th SD Meeting – Milano, Italy, November 20-21, 2015

8.19.57 57th SD Meeting – Madrid, Spain, March 18-19, 2016