

## SCIENTIFIC DIVISION

### 54<sup>nd</sup> MEETING Milano, Italy (2014 11 06-07) MINUTES (*Third Draft*)

Members:	Abbr.	Term and Time of Office
Ian YOUNG (UK) (Chair)	IY	2 <sup>nd</sup> 2014 01 - 2016 12
Philippe GILLERY (FR) (Vice-Chair)	PG	2 <sup>nd</sup> 2014 01 - 2016 12
Gary MYERS (US) (Secretary)	GLM	2 <sup>nd</sup> 2012 01 - 2014 12
Christa COBBAERT (NL)	CC	1 <sup>st</sup> 2012 01 - 2014 12
Naotaka HAMASAKI (JP)	NH	2 <sup>nd</sup> 2012 01 - 2014 12
Giampaolo MERLINI (IT)	GMI	2 <sup>nd</sup> 2014 01 - 2016 12
Joseph PASSARELLI (US) (Corporate Rep.)	JP	2 <sup>nd</sup> 2013 01 - 2015 12
David BUNK (NIST Representative)	DB	Consultant
Heinz SCHIMMEL (IRMM Representative)	HS	Consultant
Mathias MÜLLER (JCTLM Representative)	MM	Consultant

#### EXECUTIVE SUMMARY - SCIENTIFIC DIVISION 54<sup>th</sup> MEETING, MILAN, ITALY, NOVEMBER 6-7, 2014.

**Present:** Ian Young (Chair), Philippe Gillery (Vice-Chair), Gary Myers (Secretary), Naotaka Hamasaki, Joseph Passarelli (Corporate Representative), Mathias Müller (JCTLM Representative), Heinz Schimmel (IRMM Representative) and Ms Paola Bramati (IFCC Office) were in attendance. Kiyoshi Ichihara, Chair C-RIDL attended 11/06/14. Apologies received from Christa Cobbaert, Giampaolo Merlini.

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

The EFLM Scientific Committee and SD leadership agreed there should be close liaison and communication between the two groups. Elvar Theodorsson, Linköping University, Sweden, is the new Chair of the EFLM Science Committee. IY and PG met with Elvar during the IFCC WorldLab Congress in Istanbul, Turkey. EFLM has established a Working Group: Harmonising the total testing process under the leadership of Professor Ferruccio Ceriotti. The Terms of Reference of the Working Group include:

- Survey and summarize National European and Pan European harmonization initiatives.
- Promote and coordinate the diffusion of at least two especially promising harmonization initiatives among the EFLM member societies.
- Take initiatives to harmonize nomenclature, units and reference intervals on a European level.

**6.1 WORLD HEALTH ORGANIZATION (WHO):** PG attended a meeting of the Expert Committee on Biological Standardization (ECBS) at WHO, Geneva, 14-15 October 2014.

**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/](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, recognition and acknowledgement of the JCTLM and the database that it produces. The establishment of a JCTLM working group on Education and Promotion of Traceability could be effective in achieving this, and could also have the task of organizing the biennial meeting of JCTLM Members. The meeting of Members will be organized every two years and be referred to as a Members' meeting. In the future such meetings will be held in conjunction with large Lab Medicine conferences. JCTLM has organized a symposium for EUROMEDLAB 2015 titled: METROLOGY AND STANDARDISATION IN LABORATORY DIAGNOSTICS.

**6.22.2 JCGM:** WG1 (GUM) met September 29-October 3, 2014 at BIPM, Paris. 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 in September. 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)**

NIBSC contacted the SD to determine if there is interest in forming a WG to prepare new PSA material. NIBSC has purchased a large batch of recombinant PSA but is undecided how to proceed. NIBSC will convene a meeting in London in early 2015 of key advisors to obtain input on how to proceed.

#### **6.37 NATIONAL INSTITUTE FOR STANDARDS AND TECHNOLOGY (NIST):**

NIST SRM 927e Bovine Serum Albumin (7% solution) is now available.

## **8.2 MAIN ACTIVITIES OF COMMITTEES:**

**8.2.6 C-NPU:** 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. IUPAC will not produce paper editions of the 'Color books' in the future.

**8.2.11 C-MD:** IFCC received a project proposal titled: Cancer Genomics Clinical Laboratory Guidance. The objectives of the project are to: 1. survey the currently used and emerging technologies in oncology genomics, 2. survey current standards and guidelines in quality assurance and regulation of clinical genomic laboratories and 3. establish a framework to guide clinical laboratories in implementing genomics in oncology.

**8.2.21 C-RSE:** The C-RSE continues to work on two activities: 1) evaluation of the commutability of IRMM CRMs for ALT, LDH, and CK and 2) refinement of the pancreatic lipase reference method. A commutability study that included all the important manufacturers in the field and the most commonly used analytical systems was completed and a preliminary report prepared.

**8.2.23 C-TLM:** The SD has concern with the HbA1c Reference Lab Network with respect to the numerous modifications to the official IFCC Reference Method that now exist. The SD will write to JCTLM requesting the 2008 modified method be added to the JCTLM list of reference methods to make it publically available on the website. The key measurands for RELA2014 are total cholesterol, Sodium, CK, HbA1c, total protein, progesterone, digoxin, total thyroxine, and 25-OH-Vitamin D3. 'Limits of Equivalence' are added to the publication of results, if at least five reference laboratories using a JCTLM listed procedure submit their results. 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.

**8.2.25 C-STFT:** Work on final Phase IV method comparison continues. Study design for reference intervals for FT4 and TSH includes 120 samples measured with 8 immunoassay systems. FT4 also measured with ED ID-LC/tandem MS. Labs ready to provide RMP services for FT4 are UGent and the Reference Material Institute for Clinical Chemistry Standards (ReCCS).

Labs committed to develop the FT4 conventional RMP are CDC, Stanford University, and Radboud University Medical Center.

### **8.3 MAIN ACTIVITIES OF WORKING GROUPS:**

**8.3.35 WG-HbA<sub>2</sub>:** The recent activities of the WG-HbA<sub>2</sub> have mainly concerned the development of the reference measurement procedure based on isotope dilution-mass spectrometry (ID-MS). Preliminary experiments performed on a few EQAS blood samples showed the method to be feasible and reproducible. The method will be validated on hemolysates prepared from blood of healthy subjects and  $\beta$ -thalassemia carriers. With regards to the development of an alternative method for the determination of HbA<sub>2</sub> by the quantification of intact globin chains by LC-ESI/MS, a set of 10 samples and 5 calibrators were prepared and analyzed. The main difference with respect to the previous experiments was that the calibrators consisted of mixtures of high purified HbA<sub>0</sub> and HbA<sub>2</sub>. The results showed a close correlation with the HPLC method and a significant improvement in the reproducibility of the method (CV < 2.6 %).

**8.3.36 WG-CDT:** Nothing new to report since last SD meeting.

**8.3.39 WG-SAU:** All activities of the WG-SAU are a joint effort with the NKDEP Laboratory Working Group. A manuscript on the results of the albumin adsorption study has been published. Robinson MK, Caudill SP, Koch DD, Ritchie J, Horton G, Eckfeldt JH, Sandberg S, Williams D, Myers G, Miller WG. Albumin adsorption onto surfaces of urine collection and analysis containers. Clin Chim Acta 2014;431:40–45. In addition a manuscript on the status of harmonization among commercial immunoassays for urinary albumin has been published, Bachmann LM, Nilsson G, Bruns DE, McQueen MJ, Lieske JC, Zakowski JJ, Miller WG. State of the Art for Measurement of Urine Albumin: Comparison of Routine Measurement Procedures to Isotope Dilution Tandem Mass Spectrometry. Clin Chem 2014; 60:471-480. A joint meeting including NKDEP and representatives from each major manufacturer is planned for Feb 5th, 2015 at the NIH campus in Bethesda, MD. The goals of the meeting are 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. Both NIST and FDA will participate in the planning meeting.

**8.3.40 WG-PAPPA:** Activity to develop a reference system for standardisation of PAPP-A measurement employed as a marker for prenatal screening have been very slow. SD is considering closing the WG-PAPPA.

**8.3.42 WG-SIA:** Establishment of a reference measurement procedure for serum insulin is on-going.

**8.3.43 WG-TNI:** WG is collecting patient samples through R. Christenson's lab to prepare pooled reference material. Julian Barth will collect patient samples for commutability study of new pooled SRM. The Troponin and Natriuretic Peptide tables on the IFCC website will continue to be updated by the WG-TNI.

**8.3.45 WG-HAT:** Update on reference materials

- Anti  $\beta_2$  glycoprotein 1 ( $\beta_2$ GP1)
  - Long term stability and homogeneity analysis in process
  - Between vial variability is slightly higher than expected at approx. 2% and this is currently being investigated
  - Value assignment of this material is in process
- Anti myeloperoxidase (MPO)
  - Long term stability and homogeneity analysis in process – 2 year results expected in December
  - Value assignment in process
- Anti Proteinase III (PR3)
  - commutability data is complete
  - Awaiting confirmation of processing for MPO and  $\beta_2$  GP1 and then will progress.
  - value assignment to be done after Anti MPO and anti  $\beta_2$ GP1
- Anti-glomerular basement membrane antibodies (GBM)
  - To start as the Anti MPO and anti  $\beta_2$ GP1 near completion

**8.3.47 WG-cMSP:** The updated Terms of Reference are:

- To define appropriate operating procedures to perform quantitative mass spectrometry analyses for peptide and proteins from biological fluids.

- To evaluate the specification and the need for reference materials for quantitative proteomics applied to clinical biology.
- To design of a Quality Assurance / Quality Control (QA/QC) Program and to select a small series of analytes to be the subject of a future multi-site validation study.
- To test the implementation in clinical laboratories of quantitative mass spectrometry analyses for peptide and proteins, using the examples of hepcidin and apolipoproteins

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

**8.3.49 WG-CSFP:** The WG has completed a full validation, according to ICH guidelines, of the mass spec assays for CSF A $\beta$ 1-42, on a Q Exactive instrument. This project was summarized in a manuscript published in Clinical Chemistry. Andreas Leinenbach, Josef Pannee, Thomas Dülffer, Andreas Huber, Tobias Bittner, Ulf Andreasson, Johan Goborn, Henrik Zetterberg, Uwe Kobold, Erik Portelius, and Kaj Blennow , on behalf of the IFCC Scientific Division Working Group on CSF proteins. Mass Spectrometry–Based Candidate Reference Measurement Procedure for Quantification of Amyloid- $\beta$  in Cerebrospinal Fluid. Clin Chem 2014;60:987-94

**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 not sure if ASBMR will join with other groups.

**8.3.51 WG-C:** The WG-C has established four Task Forces. The WG determined the intended audience for their work output was the following groups as beneficiaries of advancing understanding and assessment of commutability of reference materials: patients, clinical laboratory, IVD industry, reference material providers, EQA organizations.

(TF1) Selecting patient specimens for inclusion in a commutability study

(TF2) Qualification of measurement procedures for inclusion in a commutability study

(TF3) Criteria to make a determination that a RM is commutable (or non-commutable).

(TF4) Statistical designs to assess commutability

## 8.19 MEETINGS

8.19.55 55th SD Meeting – Paris, France, June 19-20, 2015

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