

SCIENTIFIC DIVISION

64th MEETING Milano, Italy (October 11 and 12, 2019) 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
Barnali Das (IN)	BD	1 st 2018 06 - 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
Ian YOUNG (UK) (Chair JCTLM)	IY	Consultant
Chris BURNS (UK) (NIBSC Representative)	CB	Consultant
Greg MILLER (US) (ICHCLR Representative)	GM	Observer
To be nominated (CN) (NIFDC Representative)		Observer

EXECUTIVE SUMMARY - SCIENTIFIC DIVISION 64th MEETING, Milan, Italy, October 11 – 12, 2019.

Present: Philippe Gillery (Chair), Christa Cobbaert (Vice-Chair), Joe Passarelli (Secretary), Barnali Das, Konstantinos Makris, (Members), Karen Phinney (NIST Representative), Heinz Schimmel (JRC Observer), Ian Young (SD Consultant/Chair JCTLM), and Greg Miller (ICHCLR Representative) were in attendance. Apologies received from Mario Plebani, (Member), Jim Pierson-Perry (Corporate Representative), and Chris Burns (NIBSC 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. His second term is scheduled to conclude at the end of 2019. The Science Committee is responsible for scientific matters within EFLM and projects which further the scientific development of EFLM (except those specifically related to quality management, which are the responsibility of the Quality Management Committee). 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 consensus of the SD is that these activities do not overlap with ours. The Working Group on Test Evaluation is chaired by CC who does not believe there is much overlap as the focus is more on how to generate clinical evidence rather than on analytical standardization. PG has been in contact with the chair of the EFLM SC. Approaches to avoid overlap and work collaboratively continue to be discussed and explored. PG also met with Prof. Kilpatrick (EFLM) during EuroMedLab 2019 in Barcelona to discuss these issues further. A new Task and Finish Group will be established to address the clinical uncertainty for Medical Labs ISO document soon to be released with Prof. Graham White as the main author (ISO/TS 20914:2019: Medical laboratories — Practical guidance for the estimation of measurement uncertainty).

6.1 WORLD HEALTH ORGANIZATION (WHO):

The WHO meeting occurs each autumn. PG attends and participates as the liaison from the SD. CB is also a full member of the WHO Expert Committee on Biological Standardization (ECBS) and will be able to provide a complete update from the WHO. There was a call for public comment with respect to the WHO Model List of in Vitro Diagnostics - https://www.who.int/medical_devices/diagnostics/selection_in-vitro/selection_in-vitro-meetings/sage-ivd-2nd-meeting/en/. Comments were requested concerning the following document that was distributed to all SD members:

“WHO list of priority medical devices for management of cardiac diseases, stroke, and diabetes”

PG has the responsibility to summarize/consolidate the comments from the SD and to send them to WHO. Prof. Sverre Sandberg has been selected to represent the IFCC to the WHO on this document. The WHO will issue recommendations coming from all comments from all parties after review by the advisory panel and a 3rd version will be prepared.

6.2 CLINICAL AND LABORATORY STANDARDS INSTITUTE (CLSI):

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/).

The proposal to update the CLSI EP28 guidance document on reference ranges to reflect recent advances from IFCC C-RIDL and other content was not accepted due to the very large estimated size of the revised document. Instead, CLSI made a counterproposal to split the intended revision content into two separate documents:

- Establishment/verification of reference ranges for a single population
- Multicenter studies for expanded reference ranges across regions, nations, etc.

Dr. Ozarda, Chair of the IFCC C-RIDL, will update the proposal to focus on the first topic and submit it back to CLSI in time for the next approval meeting (Jan 2020). She will serve as the Vice-Chair of the revision project once it is approved to begin. She also will work on a proposal for the second topic to be submitted later.

The following new publication was released in 2019:

- Autoverification of Medical Laboratory Results for Specific Disciplines (AUTO15)

The following new publications are planned for release in late 2019 through 2020:

- Newborn Screening for Hemoglobinopathies (NBS08)
- Assessment of Equivalence of Sample Types (EP35)
- Point-of-Care Testing for Infectious Diseases (POCT15)
- Blood Collection on Filter Paper for Newborn Screening programs (NBS01)
- Revision to Collection of Capillary Blood Specimens (GP42)

- Collection, Transport, Preparation, and Storage of Specimens for Molecular Methods (MM13)
- Revision to the Reagent Stability Guidance Document (EP25)
- Revision to Point-of-Care Coagulation Testing and Anticoagulation Monitoring (POCT14)
- Revision to the Linearity Assessment Guidance Document (EP06)
- Revision to Collection, Transport, and Processing of Blood Specimens for Testing Plasma-Based Coagulation Assays (H21)
- Revision to the Qualitative Assay Performance Evaluation Guidance Document (EP12)

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

Summary of Major Proposed Changes in 2019 revision of the Declaration of Cooperation (DoC) document establishing the JCTLM

Rationale for Changes

1. The DoC is being revised to facilitate expansion of the JCTLM Executive Committee to include additional organizations in its membership from further branches of laboratory medicine, as was foreseen in 2016. This will allow the Committee to contribute to activities aimed at reducing the variability of measurements results in medical laboratories for a wider range of important analytes.
2. The International Council for Standardization in Haematology (ICSH) submitted its application for JCTLM Executive Committee membership in 2018, and the application was supported by the current members of the Executive.

Current JCTLM Database Content:

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

The JCTLM Stakeholders meeting will take place on December 2 and 3, followed by the JCTLM working group on new cycle submissions and then the meeting of the Executive Committee.

6.22.2 Joint Committee for Guide in Metrology (JCGM):

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

WG1 confirmed the title “Guide to the expression of uncertainty in measurement” for the whole suite. Various practical aspects, such as rebranding and renumbering the existing documents, are under discussion by WG1. This document was originally planned as supplement 3 to the GUM, under the heading “Evaluation of measurement data”. In the spirit of the new perspective on the GUM, its title was changed to: “Guide to the expression of uncertainty in measurement – Developing and using measurement models”. The new title reflects the evolution of the document since its earlier stages, when the traditional structure of the GUM and GUM-related documents was still in place, and its current status. The scope has been broadened well beyond that strictly relevant to JCGM 100:2008, and now includes statistical models and modelling of dynamic measurements. This document represents a bridge between the traditional structure of the GUM and the new perspective and is to be considered as the first document in the new structure. Having a broader scope would also allow the “new” GUM to be better harmonized with existing ISO standards.

Dr. Graham White is acting as IFCC representative.

Report from Working Group 2 (VIM)

The chair (Dr. Charles Ehrlich) of the Joint Committee for Guides in Metrology Working Group 2 (JCGM WG2) provided the following update to the SD:

WG2, in consultation with the JCGM Chairman, decided to proceed along two parallel paths:

Path 1 was to develop a new draft 'minimum change' document that starts from the VIM3 Chapters 1-5 and simplifies the language, incorporates the VIM3 Annotations and includes some agreed-upon content-related changes. In parallel, further entries on nominal properties were developed and put in a separate new chapter. The new 'minimum change' draft and the new chapter on nominal properties are now essentially ready for consultation. WG2 has focused on developing the draft 'minimum change' document ready for the current JCGM meeting, according to the mandate from the JCGM.

Path 2 was to create a new 'evolutionary' document, which possibly incorporates the expanded definition of 'measurement', and includes several other significant changes. WG2 has started down this second path as well, but it will take more time to complete a draft ready for circulation.

A copy of the minimum change "Committee Draft" document was circulated, which incorporated changes that were made at the WG2 meeting held on 26-30 November 2018. Dr Ehrlich commented that the feedback received from the circulation had indicated that the VIM4 is more "readable".

A complete draft of the "VIM4" (including the minimally revised versions of chapters 1-5 and the new chapter 6) will be circulated as a committee draft (CD) to the JCGM member organizations for their comments after the June 2019 WG2 meeting. Dr. Gunnar Nordin is serving as IFCC representative.

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):

The CCQM covers measurement standards and standardization in all branches of chemical and biological measurement science, and provides a forum where NMIs can be addressed collectively. A number of the CCQM WGs have programs in which a substantial portion of their activities is related to Laboratory Medicine, and notably for the Organic Analysis (OAWG) and Protein Analysis (PAWG) working groups. The OAWG has completed a comparison of metrology institutes with Vitamin D (D3 and D2) reference measurement procedure capabilities; this covered 7 institutes and will be published soon. The PAWG has mapped out a model system to look at the different types of pure peptide/protein types with respect to different challenges for purity assessment, with the aim of running comparisons to demonstrate NMI measurement capabilities for values assigning primary reference materials for peptides/small proteins.

The BIPM invited the IFCC-SD to a meeting of the BIPM's Consultative Committee for Metrology in Chemistry and Biology (CCQM) that was held on 10-12 April 2019 at the BIPM. Some of the decisions taken at this meeting:

- CCQM approved five Key Comparisons proposed by OAWG: CCQM-K78.b on a non-polar multicomponent solution; CCQM-K148.b on high polarity pure organics; a new Key Comparison on Zearalenone in Maize; CCQM-K154.b on aflatoxin B1 in acetonitrile and CCQM-K159 on amino acids in plasma.
- CCQM approved a proposal for a Key comparison on hydrogen purity and a Key comparison on dimethylsulphide in nitrogen at the nmol/mol level, to be coordinated by the Gas Analysis Working Group.

- CCQM approved proposals for a KC and parallel Pilot study on selenoproteins in human serum, and a KC and parallel Pilot study on anions in seawater, coordinated by the inorganic analysis working group.
- CCQM approved proposals for a pilot comparison on calibrated isotope ratio in natural copper, and a key comparison on bulk carbon isotope ratio in vanillin, to be coordinated by the Isotope Ratio Working Group.
- CCQM approved proposals for two studies to be conducted by the protein analysis working group: A Key comparison on the catalytic concentration of clinical enzymes in serum and a Key Comparison on purity of parathyroid hormone (PTH), continuing the CCQM-K115 series.

6.22.3.2 CC for Units (CCU): The IFCC is also a Member of the BIPM's CCU and was invited to attend the 24th meeting of the Consultative Committee for Units which took place at the BIPM from Tuesday 8 to Wednesday 9 October 2019 under the chairmanship of Prof. Joachim Ullrich. Professor Philippe Gillery as representative of the IFCC participated. Some of the decisions taken:

- Improve liaison between ISO TC 12, IEC TC 25, IUPAP C2, the CIPM, and its CCs for future revision of relevant standards for units. (CCU WG on units, to make a proposal)
- Add a question on implementation of revised SI within national legal metrological framework to the questionnaire for stakeholders.
- CCU WG on units to make a proposal to CCU on the definition of "unit", "quantity", "value of quantity" by end Sept. 2020, possible extension of scope to be discussed by CIPM.
- NMI members and liaison organizations to bring official opinion on definition of "unit" and units for angles and frequencies to next CCU meeting (2021).

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

The status of JRC reference materials activities are mostly covered under the respective Cs and WGs. The JRC continues to collaborate with numerous SD Cs/WGs on a variety of projects. These include:

Enzyme CRMs:

1. CRM for alpha-amylase: ERM-AD456/IFCC:

This project was finalized and the CRM was released on 2 October 2019.

CRMs for autoimmune disorders:

1. CRM for IgG anti-B2GP (antiphospholipid syndrome (APS)): ERM-DA477/IFCC
2. CRM for IgG anti-GBM (vasculitis): ERM-DA484/IFCC
3. CRM for IgG and IgA anti tissue transglutaminase (Celiac disease)

CRMs for CSF proteins:

1. CRM for A β 1-42 in CSF: ERM-DA480/IFCC, ERM-DA481/IFCC, ERM-DA482/IFCC
The CRMs were released at the end of 2017. Re-calibration of commercial assays using the CRMs has been completed. A round-robin study is currently organized to see the effect of re-calibration on the measurement results for patient samples.
2. CRM for A β 1-40 in CSF: ERM-DA480/IFCC, ERM-DA481/IFCC, ERM-DA482/IFCC
Certification project on the existing CRMs: ERM-DA480/IFCC, ERM-DA481/IFCC and ERM-DA482/IFCC.
3. CRM for Tau project: Development of a reference system for Tau
4. Neurofilament light (Nfl): Project for the standardization of Nfl in blood (possibly in CSF).

CRM for Thalassemia:

1. CRM for HbA2: ERM-DA485/IFCC and ERM-DA486/IFCC
The calibrant materials have been processed and they will be value-assigned in the coming months. The processing of the CRMs is planned for autumn 2019.

CRM for apolipoproteins:

1. CRM for Apolipoprotein(a) apo(a): and the apolipoproteins A-I, B100, C-I, C-II, C-III and E. All is under development.

6.33 NATIONAL INSTITUTE OF BIOLOGICAL STANDARDS AND CONTROL (NIBSC)

PROPOSED NEW INTERNATIONAL STANDARDS OR WHO REFERENCE REAGENTS:

1. WHO 6th International Standard for Hepatitis C virus RNA for NAT
2. WHO 1st International Standards for HPV DNA for low-risk types HPV6 and HPV11 and high-risk types HPV 31, 33, 45, 52 & 58
3. WHO International Collaborative Studies for Standardization of Ebola Virus Assays
4. WHO 1st International Standard for Anti-Mullerian Hormone (AMH)
5. WHO 1st International Standard for insulin, human
6. WHO 2nd International Standard for Anti-tetanus Immunoglobulin human
7. WHO 1st International reference panel for Cancer mutation detection
8. WHO 1st International Standard for Factor XIII Plasma. Additionally Assign Value for Total Factor XIII-B
9. Inclusion of additional Reference Reagents in the existing WHO IRR collection for blood group genotyping
10. WHO 1st International Standard for antiserum to RSV subtype A and subtype B
11. WHO 1st Repository of Red Blood Cell transfusion-relevant Bacterial reference strains

PROPOSED NEW PROJECTS:

1. WHO 6th International Standard for Chorionic Gonadotropin, Human
2. WHO 1st International Standard for Genomic EGFR Variants
3. WHO 2nd International Standard for Beta2 Microglobulin
4. WHO 1st International Standard for anti-Q fever serum (human)
5. WHO 1st International Standard for anti-Rift Valley fever Virus antibody
6. WHO 1st International Standard for Rift Valley Fever virus RNA
7. WHO 1st International Standard for detection of Replication Competent lentiviru
8. WHO 1st Reference Reagents for microbiome analysis by NGS
9. WHO 1st International Standard for Legionella urinary Antigen
10. WHO 1st International Standard for aspergillus DNA For NAT assay
11. WHO 1st International Standard and reference panel for cell-associated HIV nucleic acid
12. WHO Reference Reagent for platelet flow cytometry
13. WHO 1st International Standard for Plasma Prekallikrein & High Molecular Weight Kininogen

The list of proposed new projects represents a request from NIBSC to take these projects forward.

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:

- pre-natal serum
- TNI

- urine albumin
- materials for bone metabolism

The troponin material is in the process of being aliquoted and should be available by the end of 2019.

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. The NPU Steering Committee continues to provide governance for the NPU terminology through representation from key stakeholders consisting of IFCC, IUPAC and National Release Centre representative, while the C-NPU functions as the technical and scientific expert committee.

The annual face-to-face meeting of the NPU Steering Committee (SC) was held at the Danish Health Data Authority (DHDA) in Copenhagen on 30 September 2019. Three countries (Denmark, Norway and Sweden) use NPU extensively. Interest in using NPU terminology is growing in Finland and the Czech Republic. C-NPU recently published a paper in the eJournal of IFCC on Recommendations on measurement units – why and how? The Electronic Journal of IFCC (eJIFCC) – Vol. 30 no. 3 October 2019.

8.2.11 C-MOLECULAR DIAGNOSTICS (C-MD):

A lecture on Molecular Diagnostics was given as part of the Colabiocli 2019 in Panama. Quality considerations for molecular biology was the overriding topic, with focus on quality improvement in molecular diagnostics in Latin America. The committee also met at the Euromedlab in Barcelona. A major point of the meeting was the discussion of the results of the latest survey, which was carried out at the end of 2018. For the first time a web-based international survey was conducted about Survey monkey in two languages (Spanish and English), which addressed among other things the effort for quality assurance in the laboratories. A total of 93 laboratories took part in the survey and the results were presented at congresses. A manuscript showing the results of the survey will be submitted to the SD by the end of 2019. An additional survey in Arabic is planned and will contain above all aspects covering the external quality control and alternative assessment procedures.

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

The annual meeting 2019 was held in Barcelona on May 20, 2019. All members of the committee as well as several corresponding members, corporate members and guests were present. The next meeting will take place in Seoul, Korea during IFCC Worldlab on May 2020.

RELA:

The results of RELA2018 have been evaluated and published (<http://www.dgkl-rfb.de:81>). The number of published results is constantly increasing up to approximately 500 results of 50 laboratories. Especially laboratories from Europe and China are active in the project. Total hemoglobin is part of RELA measurands for the first time. Four laboratories submitted and published their results. The next RELA survey has been announced. Participants reported that there was an increasing need for clarification regarding the naming of the survey. Therefore, it was decided to equate the name of the

execution with the year of the certificate issuance. Thus, RELA 2020 is hereby announced; a survey called "RELA 2019" will not take place. The samples will be shipped in November 2019 and the survey period will end in April 2020. The measurands remain the same as for RELA 2018.

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

A meeting was held on May 19th 2019 during the 23rd IFCC-EFLM European Congress-EuroMedlab Congress in Barcelona. At the meeting, the topics/planned publications of the C-RIDL were discussed and decided as below:

1. Comparison of direct and indirect reference intervals of Turkish data
2. Japan direct/indirect studies, and a proposal for a validation project
3. The different indirect methods with primary care patient data
4. Von Willebrand factor multimers and their reference intervals in Estonia
5. Reference intervals of hematological parameters for Nepalese population
6. Training and Education on the use of indirect methods
7. Recent activities in common reference intervals and decision points in Australia
8. Proposal toward the revision of CLSI guideline EP28

The CLSI Consensus Council rejected the proposal given by C-RIDL. The major concern was the eventual length of the guidance document, which was deemed too long. According to feedback provided, the document should be split into two parts; 1) verification of the reference intervals and 2) multicenter trials to establish reference intervals. The chair of C-RIDL (Prof. Yesim Ozarda) will send a revised project proposal prior to the next meeting of the CLSI Expert Panel in January 2020.

The next C-RIDL meeting will be held on May 23rd, 2020, during the IFCC WorldLab in Seoul. This meeting will be the opportunity to discuss:

- 1) Comparison of alternative approaches (conventional and big data) for the determination of reference intervals
- 2) The update to CLSI Guideline EP28-A3
- 3) Review of major papers published using indirect studies

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

Establishing a system to maintain traceability of free thyroid hormone and TSH measurements has been completed and now the focus is on implementation:

- Conducted first interlaboratory comparison study in August 2019:
 - Study contains 40 samples from hypo-, eu- and hyperthyroid individuals; awaiting results from laboratories
 - Received new serum-based reference materials from NIST for value assignment by IFCC Network. Materials are included in ongoing network study. This will be the first time that target values determined by IFCC C-STFT are used with NIST materials.
 - Japan – Working on assigning target values to reference materials from the Japanese Committee of Clinical Laboratory Standards. Values will be linked to the IFCC reference system.
 - Japan (JCCLS) will work with national societies and manufacturers to harmonize TSH with traceability to IFCC system.
 - U.S. (CDC) is working with the College of American Pathologists (CAP) to further improve the CAP accuracy-based thyroid assay.
 - U.S. (CDC) is developing certification program for free T4 traceable to the IFCC system.

Plan in-person meeting at University of Ghent November 6-7, 2019.

Agenda:

- Discuss results from network study
- Discuss network rules and cRMP SOP
- Prepare for collecting samples for 3rd TSH panel
- Provide updates on national/regional standardization and harmonization activities
- Provide updates on reference interval activities

Current Challenges:

1. Ensuring stable and consistent free T4 measurements within the laboratory network
2. Improving communication and interactions among working group members

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

Adoption of ERM-DA476/IFCC and ERM-DA483/IFCC:

September 2019 – informal meeting with the autoantibody companies at the Dresden autoantibody meeting. Two reference materials have been available for at least 2 years, however, no company so far has moved forward for standardization of their assay.

When asked the reason of not wanting to implement, the single most important element given was the cost, estimated to be \$500,000 – 1,000,000. In addition, the need to establish new verification and validation, reissuing all new documentation worldwide, FDA submission, and clinical studies were also highlighted.

New reference materials in planning or preparation:

CRM in preparation/evaluation by IFCC C-HAT and JRC

Anti B2 GP1:

Material prepared and bottled but issue with value assignment. Drs. Jo Sheldon and Evi Monogioudi (EM) from JRC met with NIBSC to explore the possibility of the material being value assigned in IU. EM has proposed this to the JRC and preliminary data has been exchanged.

Anti GBM:

Candidate raw materials have been sourced and currently being processed.

Anti TTG:

Candidate raw materials have been evaluated and are going to be purchased by the JRC.

CRM in preparation/evaluation by NIBSC:

Anti dsDNA

Anti CCP

Rheumatoid Factor

NIBSC – B2GP1 reference preparation value assignment:

UKNEQAS and RCPAQAP – agreed to accept results in mg/L calibrated w.r.t. ERM-DA476/IFCC and ERM-DA483/IFCC.

The Chair to participate in EULAR Task Force on autoimmune diagnostic tests for AARD.

Next Meeting:

Plan for a C-HAT phone conference in November 2019:

Plan evaluation of anti GBM and anti TTG materials

8.2.27 C-BONE METABOLISM (C-BM):

The Committee was constituted in January 2019 after the closure of three previous WGs (PTH, Bone Markers, and Vit D).

PTH standardization:

- Commutability study: The first step is to prove that the WHO IS 95/646 is commutable. This is still in process.

- RMP for PTH: Dr. Candice Ulmer presented the first results of the RMP LCMS/MS method on which she is currently working at the CDC facilities. She presented the updates of her methods in Barcelona and during two brown bags sessions in Anaheim at the 2019 AACC. She is working on improving the LOQ of the method and expanding the number of fragments recognized by the method. She also plans to work on real patient clinical samples.

Bone markers assays:

PINP:

A paper on the results of the multicentre study has been accepted by CCLM. During the IOF-IFCC held in Paris on April 3 2019, the chair of this C proposed an equation to “recalibrate” the kits against each other based on 10% of the results of the multicentre study. This equation has been “validated” on another set of independent. With the help of Dr. Vincent Delatour, a preliminary commutability study will be organized in Liege.

CTX:

A paper on the multicenter study has been written, but not finalized.

A study on biological variation of CTX on remaining samples from EuBIVAS has been performed.

Other bone biomarkers:

Different biomarkers have been measured in Liege to evaluate their biological variation: osteocalcin and FGF-23.

Vitamin D metabolites assay standardization:

In collaboration with the NIST, a study has been organized to evaluate the performance of different assays on a single donor panel. The LCMS reference method of NIST has been used to assign the value of the samples and they have all been measured in Liege with most of the different immunoassays available on the market according to the VDSP protocol. A paper is currently under redaction.

The lab of the chair of this C (Prof. E. Cavalier) is measuring 25OHD and 24,25(OH)₂D in samples from EuBIVAS. A manuscript is planned.

Two meetings are planned for next year:

- Meeting in Seoul during WorldLab
- Meeting with IOF WG in Barcelona in 2020 during IOF-ESCEO meeting

8.3 MAIN ACTIVITIES OF WORKING GROUPS:

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

A joint committee with ICSH (The International Council for Standardization in Hematology) is being formed. The following is a short update of the current status of activities:

1. **Candidate reference measurement procedure for HbA₂:**

The experimental work to prepare the second paper on the method with HPLC-IDMSMS is at present under pause, but it will start again soon. The recombinant hemoglobins to be used for calibration were produced by Trenzyme GmbH during this summer and delivered to the laboratory of Dr. Arsene by mid-September. Experiments to assess the purity and the content are under way. Afterwards, the remaining experiments will be performed in order to prepare the final version to be submitted to the SD EC for approval and for the ballot before publication.

2. **Certified reference material for HbA₂**

The supply of fresh blood to prepare the large batches is scheduled between October and March 2020. Consequently, the tests planned by the JRC will be organized in order to characterize these materials.

3. **IFCC-ICSH joint group on standardization of HbA₂:**

The Committee keeps constant contact with the ICSH group, by teleconferences

every 3-4 months. In the last meeting of 17 September, Prof. Mosca took the action to prepare a roadmap for the standardization of HbA₂. This will be presented at the JCTLM meeting in Paris early December, and will be object of a publication on the next special issue of CCA. The approach is to avoid the issue that happened with HbA_{1c} with respect to different reporting units. In addition, the information provides guidance to what manufacturers are supposed to do.

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

The following is a summary and a description of the current focus of this WG:

1. JCTLM Recognition of the RMP: The document was updated once again with new information after the original submission was rejected and resubmitted. The method was originally rejected mostly due to how the measurement uncertainty was calculated. The WG and JCTLM are in discussion and it is hoped that a resolution will be decided in December and the method listed in 2020.
2. There have also been communication and updates requested from commercial manufacturers towards final development and release of their CDT_{IFCC} methods. Most of them transitioned to CDT_{IFCC} early 2018. Sebia, Helena Biosciences, Biorad, Recipe and Siemens offer CDT_{IFCC} or traditional classic and IFCC results. Expression of interest to participate recently came from Chromsystems.
3. Current laboratories for the HPLC RMP are: Sweden, The Netherlands, France, United States, Italy and United Kingdom.
4. Sustainability and performance of network labs - Annual IFCC Study cycles: The robust scheme has maintained active participation by approved and candidate network laboratories. The 2019 Cycle took place during the first quarter of the year with participants' results submitted by end March. Performance and participation were presented and discussed during the meeting on 19 May in Barcelona. In brief, there were five successful IFCC networked laboratories this year, with two candidates yet to improve performance.
5. WG members have been raising awareness of CDT_{IFCC} with local authorities at regional level. Nonetheless, there is still a monumental need to raise awareness of the benefits of CDT_{IFCC} (let alone the classic version), educate those testing centres likely to provide a service and supporting members of the WG to help achieve some of these tasks. The scientific work is completed, but as one appreciates, the more holistic approach to the relevance of the test has yet to be achieved.

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.

Reference measurement procedure for UA (funded by NKDEP and NIST):

NIST and Mayo continued the development of their candidate reference measurement procedures and conducted planning sessions for validation and JCTLM submission. The funding contract for development of the reference measurement procedure at Univ of Minnesota in the Advanced Research and Diagnostic Laboratory was finalized in the beginning of March 2019. Initial studies and measurement procedure development are currently underway. In previous discussions with the NKDEP-LWG, it was agreed upon between Mayo Clinic and the University of Minnesota that a synthetic urine matrix would be utilized for calibrator preparation to ensure lot-to-lot calibrator consistency and long-term availability. The matrix would not consist of a proprietary commercial synthetic material or materials; rather it will be a matrix that can be prepared in the laboratory from commercially available chemicals.

NIST is using SRM 2925 for calibration of their candidate reference measurement procedure and has provided some guidance on linking the concentrations of calibrators at Mayo Clinic and the University of Minnesota to SRM 2925. Next steps involve consensus on alignment of calibration between laboratories with the use of the NIST reference material, performing sample comparison studies and proceeding with the validation of the reference measurement procedure.

The group has reviewed the JCTLM submission requirements and is designing validation and round robin sample exchanges to fulfil the submission requirements.

NIST and Mayo will continue to develop and validate their reference measurement procedures and will work identifying sources of disagreement among the methods, and pursue validation of the candidate reference measurement procedures in accordance with ISO 15193 and other relevant standards for JCTLM listing.

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. Documentation is currently in review in the NIST Office of Reference Materials, and official release is anticipated near the end of 2019. 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. Value-assignment of SRM 3666 for urine albumin and creatinine will be conducted by NIST. The WG-SAU will continue to facilitate development of NIST SRM 3666.

A joint IFCC/WG-SAU meeting is planned to be held in conjunction with the AACC Annual meeting in August 2020

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

The WG main goal is to harmonize the PAPP-A measurements of the various methods commercially available.

1. The most urgent challenge is the need for a PAPP-A reference material with proven commutability between the commercial PAPP-A assays for Down syndrome screening, as there has been nothing to replace the old serum-based WHO IRP that has not been available for a long time.
2. Previously WG-PAPP-A has shown that harmonization of the commercial PAPP-A assays can only be reached with pooled serum based materials (recombinant or purified endogenous products do not work).
3. The future plans of the WG include exploring a new NIST SRM 1949 as a reference material for PAPP-A assays. NIST is willing to cooperate with WG-PAPP-A to add PAPP-A reference values to the SRM certificate. Currently the PAPP-A values reported by the commercial assays are in two “pools” as mIU/L or in divergent units. The aim is to unify all assays to averaged concentration value at the same unit (or to provide a certified conversion factor to the divergent unit). SRM 1949 has now become available to enable proceeding with this task.

8.3.41 WG – GROWTH HORMONE (WG-GH)

The overall goal of the WG-GH is to achieve standardization of growth hormone through secondary reference materials and a reference measurement procedure.

A long recognized problem in the reliable measurement of GH is the lack of standardization of different assays that are currently used. Standardization of the GH assays has been hampered by the unavailability of a commutable certified reference material and of an acknowledged reference method. The WHO standard IS 98/574, against which all current assays are calibrated, was found not to be commutable when tested in different matrices. An alternative approach would be to use serum pools. In the

Netherlands, a native serum pool obtained from healthy volunteers after exercise has been used as a commutable calibrator to establish a harmonization factor for the different growth hormone assays. Using this harmonization factor, a reduction in interassay coefficient of variation was realized from 24.3% to 14%. Follow-up studies will investigate the commutability of different potential calibrators based on native, or spiked, serum pools. If a commutable calibrator is identified, an IS 98/574 calibrated LC-MSMS method could be used as a reference method to assign a value to the calibrator, allowing for IS 98/574 traceable standardization of the different GH assays.

Aim of the present survey: to establish if a commutable calibrator for the standardization of human growth hormone assays can be made from pooled human serum samples or from the international standard dissolved in a human serum matrix.

The results of the Isotope Dilution-Mass Spectrometry (IDMS) GH measurements, an antibody independent method measuring the 22 and 20 KDa separately is currently in process. Preliminary results showed that only at relatively low concentrations commutable calibrators can be made. Future direction of investigation will be the use of more fresh samples, in order to keep the native forms of GH preserved in the samples.

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.

Current status:

1. Ongoing development and validation of MS/MS method for intact insulin at University of Minnesota. Significant progress has been made following prioritization and financial support for development of the LC-MS/MS insulin assay at the University of Minnesota.
2. Continued collaboration with other laboratories (Quest Diagnostics, Mayo Clinic) developing insulin methods by mass spectrometry and sustained efforts to evolve reference method procedures in these laboratories.
3. In collaboration with the College of American Pathologists (CAP), established criteria for ongoing accuracy based evaluation of serum pools for testing of insulin, C-peptide, and glucose.
4. Continued collaboration with NIBSC to evaluate the insulin candidate reference material which will ultimately be utilize to calibrate the mass spec method and establish it as a higher order reference method.

Future Plans and activities:

1. Implement accuracy based proficiency testing survey using serum pools for insulin (and c-peptide) via the College of American Pathologists; results will allow for assessment of comparability of results across assays, using a commutable matrix, as the WG moves towards standardization or harmonization.
2. Working group report or peer-reviewed publication regarding either insulin/c-peptide serum pool data across hundreds of laboratories/assays and/or lack of harmonized conversion factor across insulin assays.

The WG met at the AACC Annual Meeting, Anaheim, CA in August 2019.

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

The WG-TNI had a productive meeting on August 5th in Anaheim at the 2019 AACC Annual Conference. The WG meeting was attended by 12 individuals, several of whom are part of the IFCC Scientific Division leadership.

The focus of the WG's efforts has been high-sensitivity cardiac troponin I assays (hs-cTnI) since it is believed this is the future of the cardiac biomarker field. The WG had an active discussion on the path forward for use of RM 2922, and for how the materials could be

employed to improve harmonization of hs-cTnI measurements. There was universal agreement that the best situation would be assignment of cTnI values to RM 2922. It would be possible then that the numerical values of the materials could be used to harmonize hs-TnI measurements so that they would be as close as possible. The feeling of the group was that true standardization of cTnI assays would only be possible with the technological development of methods, such as LC-Tandem MS, with improved detection sensitive enough to evaluate very low cTnI concentrations.

The group in attendance also discussed what requirements the US FDA might have for conversion of current hs-cTnI assays to different calibration values. Part of the discussion focused on the efforts of metrology experts who are working to harmonize thyroid testing, and have some success with moving forward. It seems clear that common cohort serial samples from suspected myocardial infarction patients could be a useful tool. Samples from myocardial infarction patients for use in producing RM 2922 continue to be collected under an Institutional Review Board protocol discussed. Currently there is approximately 0.75 litres of serum from 49 troponin I positive subjects of cTnI that is sufficient to initiate production of RM2922.

8.3.49 WG – CSF Proteins (WG-CSF):

The WG is in contact with NMIs for the standardization of the Tau proteins. There seems to be some coordinated activities. So far, the following have been accomplished:

- Two RMPs for CSF amyloid β 1-42 have been published and approved by the JCTLM (C12RMP1 and C11RMP9).
- A method for measurement of CSF amyloid β 1-40 by SRM has been published and validation of a RMP is ongoing.
- Mass spectrometric methods for measurement of CSF tau have been developed by several work group members.
- Three CRMs for CSF amyloid β 1-42 have been developed (ERM®-DA480/IFCC, ERM®-DA481/IFCC and ERM®-DA482/IFCC).
- Collection of CSF for development of CRMs for tau is ongoing.
- Round-Robin study of CSF-amyloid beta 1-42/1-40 ratio RMPs by mass spectrometry is in the planning stage.
- Round-Robin study of CSF tau RMPs by mass spectrometry is being planned.
- There has been reluctance by industry to adopt the new reference system and the WG has prepared training materials and trying to move this forward.

8.3.51 WG – Commutability (WG-C):

A manuscript titled: "IFCC working group recommendations for correction of bias caused by non-commutability of a certified reference material used in the calibration hierarchy of an end-user measurement procedure" has been reviewed and approved by SD, JRC, NIST, New York and is awaiting approval from CDC. When approval is obtained from CDC, the manuscript will be submitted to Clinical Chemistry. The manuscript includes examples in supplemental data that describe in detail how a correction for non-commutability can be performed.

WG-C will next begin to address the following items: (1) how to establish criteria for a commutability assessment; (2) verifying commutability for a replacement batch of a reference material.

As decided at the last SD meeting, WG-C will be discontinued at the end of 2019. A project proposal was submitted to the SD to begin a new WG - Commutability in Metrological Traceability that will continue to pursue the remaining objectives for the WG. This is pending EB approval. If approved, the name of the new WG will be:

WG Commutability in Metrological Traceability – (WG-CMT).

8.3.53 WG – Immunosuppressive Drug (WG-ID):

The WG is devoted to the establishment of candidate reference procedures and reference materials for immunosuppressive drugs (ISDs) such as cyclosporine, sirolimus, tacrolimus, everolimus, and mycophenolic acid (MPA).

In the discussion following the presentations, the audience came to several agreements, which will serve as basis of future undertakings:

- There is a definitive need to bridge the traceability gap between primary and secondary reference materials and the industrial master calibrators.

- At least two quality levels of procedures must be provided to allow on the one hand the characterization of highest order reference materials and on the other hand, to support industry and other stakeholders with measurement platforms allowing to characterize sample cohorts of different study settings (e.g. instrument comparison studies ...).

- JCTLM listing of reference methods and materials is a must for the WG outcome to be successful.

- qNMR is most likely the key technology to provide reference materials of unmet quality and that any reference measurement procedure must be published such, that a sufficiently qualified laboratory is in the position to participate in a reference measurement network to be defined as ultimate goal of our initiative

Dr. Loralie Langman as Past President of the IATDMCT took up the task to establish a link between IFCC and IATDMCT.

Consequently a "memorandum of understanding" to extend the WG-ID to a IFCC-IATDMCT joint WG was prepared. This memorandum is already agreed on by the IATDMCT President (Dr. Teun van Gelder) and President-Elect (Yusuke Tanigawara) and has been recently forwarded to the SD-chair for approval and forwarding to the IFCC EB.

Next meetings of the WG-ID will be held at the Worldlab 2020 in Seoul and the EuroMedlab 2021 in Munich. It is envision to organize joint presentations with the C-TLM, since JCTLM registration of established materials and methods is a central milestone of the WG-ID work. Furthermore, the WG plans to make a presentation at the IATDMCT conference 2021 in Banff – hopefully this will be the inauguration meeting of the IFCC-IATDMCT joint WG.

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.

Reference measurement procedure: in 2019, the digestion conditions have been optimized to obtain stable digestion for apolipoproteins CI and CIII. Using a stepwise digestion protocol in which proteins are first cleaved roughly into larger peptides, followed by a more precise digestion using trypsin to achieve the final tryptic peptides. This strategy was initially developed at the LUMC site, and is now successfully transferred to the calibration laboratories of the CDC and UKL.

A common draft SOP has been developed for the MS-based cRMP by the three laboratories, based on the optimized digestion conditions, as well as the parameters previously harmonized amongst the three laboratories.

An experimental plan has been designed to assess the current state of harmonization amongst the three calibration laboratories using the harmonized draft SOP

Reference materials: three-step approach has been agreed upon; first to work on materials for apo(a), then apoA-I and B, followed by materials for apoCI, CII, CIII and E. For the first apo(a) RM, in 2019, test batches of synthetic peptides have been ordered from two suppliers, and were received. It has been established that there are no interferences in the signals of the MRM transitions. Samples have been distributed to JRC and LNE and preliminary amino acid analysis as well as purity assessment will be performed before the

end of 2019. Sourcing of the peptides for apoA1 as well as apoB has been initiated, and will be finalized by Q1 2020.

Potential secondary reference materials have been identified for apo(a). Pig plasma containing defined apo(a) with a single number of kringles IV type 2 was procured and an experimental plan was developed for the purification of apo(a) from this material. Purification at an initial batch level is expected to be finalized by the end of 2019. An alternative source of apo(a) reference material could be recombinant apo(a) expressed in human HEK cells. The group aims for submission of two manuscripts in 2019, and the initiation of preparation of a third manuscript.

1. A first manuscript will outline the WG's approach on standardization of apolipoproteins.
2. A second manuscript will be a technical note or letter on the improved digestion of apolipoproteins using a combination of lysC and trypsin.
3. A third manuscript that will be in the preparation phase by the end of 2019 is the development of a harmonized LC-MS based method, including results from the planned ring trial.

8.3.55 WG – Pancreatic Enzymes (WG-PE):

The focus of the WG is developing a reference system for pancreas amylase in serum. Successful investigations covered the following:

- Determination of inhibitory constants for pancreas and salivary amylase by mAb's
- Spiked solutions: Comparison of calculated vs. experimentally determined enzyme activities
- Serum pool: Comparison of calculated vs. experimentally determined enzyme activities
- Absorption kinetics
- Correlation to total amylase activities measured in the clinical routine laboratory (n = 51)
- Correlation to lipase activities measured in the clinical routine laboratory (n = 51)
- Influence on the inhibition of glucosidase by matrix due to adding inhibitory mAb's

Two other laboratories (Francesca Canalias, Spain and Friederike Weber, Roche, Germany) performed reproduction of the investigation protocol.

Theoretical work was done by Ferruccio Ceriotti, who was listing the uncertainty budget and roughly estimating contributions of each uncertainty component. The estimated measurement uncertainty is required to discuss if the needs for a reference system can be met. A basis for discussion is the next step, namely an inter laboratory comparison of e.g. 4-5 reference laboratories and the potential source of sufficient sample material.

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

The group continues to meet twice a year and has outstanding engagement from both members and manufacturers. Typically, 20 or so people are at each meeting.

A new member to the group has joined from Canada and this is the first active member from North America.

The WG is holding their next (6th) meeting on October 18th, 2019 in Barcelona to coincide with the world endoscopy organization meeting, which is a meeting most of the members will be attending anyway.

Progress is going well with respect to the terms of reference:

- a. Standardization/ harmonization – A study already completed confirmed that standardization would probably not be possible. The group is now working towards

harmonizing to a single reference material. The JSCC have taken the lead on this on behalf of the group and will be receiving results from the latest manufacturers' product comparison study mid-October.

b. EQA material – A study that has been carried out to evaluate a number of different EQA schemes has been completed. The different EQA schemes use different sample types e.g. faecal like matrix or lyophilized samples. Based on the study results the group will provide opinion as to what is the most appropriate type of EQA sample.

c. IQC material - There is no third party IQC material available. All 4 main FIT manufacturers agreed to allow a study to take place where their IQC material was tested on all the other manufacturers' instruments. The results of this will be reported at the meeting in Barcelona that should help decide on a strategy for making 3rd party IQC available by manufacturers selling their products to labs using other manufacturers IQC.

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

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

The chair and WG have prepared a paper about the pre-analytical aspects and the paper is currently being reviewed by the WG. The chair believes the WG members will provide expertise in lung cancer, organ rejection, and other broad areas (such as exosomes). The WG also plans to be involved early on with NMIs.

8.3.58 WG – Procalcitonin (WG-PCT):

The following is the status of WG-PCT to date:

Objective 1: Develop and validate a reference measurement procedure for PCT absolute quantification by stable isotope dilution mass spectrometry (SIDMS) in order to establish metrological traceability of results to the SI Units:

- For now, the IDMS reference method will measure total PCT (PCT 1-116 + PCT 2-116 + PCT 3-116)
- Different primary calibrators (peptides and recombinant protein) have been produced. Their purity is being characterized by high resolution mass spectrometry
- Different separation methods to purify PCT in biological samples are under development and will be compared
- Suitability of recombinant PCT and/or synthetic peptides as possible primary calibrators is being investigated. Results obtained so far suggest that protein-based calibrators should be preferred to peptide-based calibrators.
- Validation of a candidate reference measurement procedure for absolute quantification of PCT by IDMS is almost achieved with peptide-based calibration. Still, measurement uncertainty and limit of quantification should both be improved because PCT concentration below 1ng/mL cannot be measured in the current state. This will be addressed with the work on protein-based calibration that will be initiated

in October 2019. The objective is to reduce measurement uncertainties and other sample preparation techniques will be deployed to improve the limit of quantification. Objective 2: Document and understand the variability of results provided by the different commercially available PCT assays:

- Leftovers from patients with different PCT concentrations (frozen serum) have been collected in different hospitals with the objective to prepare pools. Pilot pools were successfully obtained but collection of clinical specimens is continued to produce larger pools.
- Various EQA providers were approached to include their EQA materials in the study and have different types of matrices involved.
- Discussions on the design of the commutability study have started.
- An EQA scheme relying on commutable materials will be organized after study materials have been prepared and commutability is demonstrated.
- Each assay manufacturer is expected to provide preliminary information on how their assay is calibrated and what epitope is targeted by antibodies
- A decision whether standardization is needed or not will be made after the variability of results provided by the different commercially available PCT assays has been documented and understood.

The last meeting of IFCC WG-PCT took place on May 20th 2019 during EuroMedLab Barcelona.

8.3.59 WG – Continuous Glucose Monitoring (WG-CGM):

This is a newly formed working group and the first meeting will take place in October.

Terms of Reference:

- Establish traceability of glucose values obtained by continuous glucose monitoring (CGM) to materials and methods of higher metrological order
- Establish metrics for the evaluation of the analytical performance of CGM
- Work with ISO on a new CGM guideline (analogous to ISO 15197) to establish standardized procedures and acceptance criteria for CGM

Current projects:

- Propose means suitable for establishing the traceability of glucose values obtained by CGM to materials and methods of higher metrological order according to ISO 17511, including definition of adequate compartment(s) for reference samples (capillary, venous)
- Find procedures suitable for assessment of analytical performance of CGM systems
- Define metrics and corresponding minimum acceptance criteria for the analytical performance of CGM systems

8.19 MEETINGS

- 8.19.64 64th SD Meeting – Milano, Italy, October 11th and 12th, 2019 at the IFCC office.
- 8.16.65 65th SD Meeting – May 27th and 28th, 2020 in conjunction with WorldLab 2020 – Seoul, South Korea
- 8.16.65 66th SD Meeting – tentative in October 2020 at the IFCC offices in Milano