

Prof. dr. C.M. Cobbaert, EuSpLM

Vice-chair of IFCC SD

**Department of Clinical Chemistry & Laboratory
Medicine, LUMC, Leiden, the Netherlands**



IFCC

*International Federation
of Clinical Chemistry
and Laboratory Medicine*

SD Report to IFCC Council

P. Gillery, *Chair*



April 10th, 2022

Twenty Forth Triennial meeting of Council

ifcc.org

IFCC-SD Scientifique Division (SD) : Missions

To advance the science of Clinical Chemistry and to apply it to the practice of Clinical Laboratory Medicine

- **By identifying technical innovations** and diagnostic strategies and assisting the transfer of these to the profession
- By promoting **the standardization of laboratory tests** and the **comparability of patient results** through the development of reference measurement systems, or harmonization activities where standardization is not yet possible
- **By establishing standards** for scientific and technical aspects of **good laboratory practice**
 - **Executive Committee**
 - **7 Committees (theme oriented)**
 - **17 Working Group (task oriented)**

IFCC-SD Executive Committee

Name	Position	Country	Term	Time in Office
P. Gillery	Chair	FR	2nd	2020 01 - 2022 12
C.M. Cobbaert	Vice-Chair	NL	2nd	2020 01 - 2022 12
G. John	Secretary	UK	1st	2021 03 - 2023 12
B. Das	Member	IN	2nd	2021 01 - 2023 12
K. Makris	Member	GR	2nd	2020 01 - 2022 12
M. Plebani	Member	IT	2nd	2020 01 - 2022 12
M. Rottmann	Corporate Member	DE	1st	2020 03 - 2022 12
R.D. Josephs	BIPM Observer	FR		
L. Deprez	European Commission/JRC Observer	BE		
I. Young	ICHCLR Observer	UK		
G. Miller	JCTLM Chair / SD Consultant	US		
C. Burns	NIBSC Consultant	UK		
Y. Zhen	NIFDC Observer	CN		
K. Phinney	NIST Consultant	US		

Main drivers for setting up of a SD working party ?

SD horizon scanning

Third party approach

- Assessment of clinical needs
- Determination of priority (cooperation with ICHCLR)
- Development and submission of formal proposal
- Agreement on terms of reference

Approval by SD and EB
Establishment of WG or C

Work cycle with ongoing review

- state of the art
- definition of the measurand
- availability of "pure" reference materials
- possibility of "standardization" vs "harmonization"

7 IFCC-SD Committees (Theme-oriented)

- Nomenclature, Properties and Units (C-NPU) in collaboration with International Union of Pure and Applied Chemistry (IUPAC) Y.B.L. Hansen (DK)
- Molecular Diagnostics (C-MD) P. Ahmad-Nejad (DE)
- Traceability in Laboratory Medicine (C-TLM) A. Kessler (DE)
- Reference Intervals and Decision Limits (C-RIDL) T. Streichert (DE)
- Standardization of Thyroid Function Tests (C-STFT) H. Vesper (US)
- Harmonization of Autoimmune Tests (C-HAT) J. Sheldon (UK)
- **Bone Metabolism (C-BM)** **E. Cavalier (BE)**

17 IFCC-SD Working Groups (Task oriented)

- Standardisation of Haemoglobin A2 (WG-HbA₂)
 - **Standardisation of Carbohydrate-Deficient Transferrin (WG-CDT)**
 - Standardisation of Albumin Assay in Urine (WG-SAU) in collaboration with NKEDP
 - Standardisation of Pregnancy-Associated Plasma Protein A (WG-PAPP A)
 - Growth Hormone (WG-hGH)
 - Standardisation of Insulin Assays (WG-SIA) in collaboration with ADA/EASD
 - Standardisation of Troponin I (WG-TNI)
 - CSF Proteins (WG-CSF)
 - Commutability in Metrological Traceability (WG-CMT)
 - **Immunosuppressive drugs (WG-ID)**
 - Apolipoproteins by mass spectrometry (WG-APO MS)
 - Pancreatic enzymes (WG-PE)
 - **Fecal Immunochemical Testing (WG-FIT)**
 - Cell free DNA and related biomarkers (WG-cfDNA)
 - Standardization of Procalcitonin assays (WG-PCT)
 - **Continuous Glucose Monitoring (WG-CGM)**
 - Development of a Reference Measurement System for sustainable PT/INR Standardization
- A. Mosca (IT)
 - J. Deenmamode (UK)**
 - J. Seegmiller (US)
 - S. Wittfooth (FI)
 - M. Vos (NL)
 - M. Steffes (US) & J. Seegmiller (US)
 - R. Christenson (US)
 - J. Gobom (SE)
 - G. Miller (US)
 - C. Seger (CH)**
 - C. Cobbaert (NL)
 - D. Grote-Koska (DE)
 - S. Benton (UK)**
 - R. van Schaik (NL)
 - V. Delatour (FR)
 - G. Freckmann (DE)**
 - C. Cobbaert (NL)

WGs close to completion :

- **WG-HbA2** in collaboration with ICSH (International Council for Standardization in Haematology) **Chair : Prof. A . Mosca (IT)**
 - "Old" WG - Important topic in public health
 - Development of RMP
 - Activities to complete (Roadmap : in *CCA 2021 ; 512 : 185-190*)
 - Finalization of HbA2 RMP ⇨ ballot for IFCC RMP endorsement and then JCTLM listing
 - Commutability of CRMs
 - Value assignment by reference laboratories - Maintenance of RMP lab network
- **WG-CDT (Carbohydrate-Deficient Transferrin)** **Chair : Dr Jean Deenmamode (UK)**
(F. Schellenberg (FR) , JPM. Wielders (NL), Members)
 - Promoting the use of the HPLC reference measurement procedure (RMP) as the accuracy base for CDT test standardization = **IFCC-RMP for CDT established in 2016**
 - Maintaining sustainability of an international network of reference laboratories
 - Supporting the worldwide standardization of commercial methods against the RMP
 - **Current action = JCTLM listing of the IFCC-RMP as Reference Method**

Working Groups : Highlights

- **WG-CMT (Commutability in Metrological Traceability) Chair : Dr Greg Miller (US)**

Commutability of reference and control materials : a major concern in Lab. Med.

- **Establish procedures** to use commutable reference materials, and to correct for non-commutability bias, in a metrological traceability hierarchy.
 - **Establish how to define the criterion for acceptable commutability** for a given reference material
 - **Provide recommendations on verifying commutability** for replacement batches of a reference material.
- **WG-APO MS (Apolipoproteins by Mass Spectrometry) Chair : Prof. Christa Cobbaert (NL)**
 - Ambitious project of **Apo standardization (apo) A-I, B, C-I, C-II, C-III, E and apo (a) with traceability to SI (ISO 17511)**
 - LC-MS/MS-based reference unaffected by genetic variants, post-translational modifications and other factors.
 - Involvement of NMIs (LNE/PTB) through the CardioMet project and future CardioMet 2 (EMPIR programme funding)
 - Preparing the transition from WHO-IFCC RMS to JRC/IFCC RMS for apo(a), apoA-I and apoB standardization (cave: discontinuation and closure of the sole responsible reference lab)
 - Two manuscripts in preparation almost ready for submission
 - Commutability study for apo(a)
 - Candidate LC-MS based reference method

Working Groups : Highlights

- **WG-PCT Chair : Dr Vincent Delatour (FR)**

- Active involvement of Metrology Laboratories (with specific resources)
- Development of all tools requested for standardization on metrological basis (RMP (ID/MS,) Materials)
- **Challenges : shared by several Cs or WGs**

PCT assays will be standardized :

- *if the ID/MS method meets the necessary performance specifications,*
- *if the variability of results provided by the different commercially available PCT assays is considered unacceptable and can be improved through common calibration with commutable secondary calibrators*
- *if correlation between the ID/MS method and routine assays is sufficient*
- *if most assay manufacturers agree recalibrating their assay*

- **WG-PT/INR (Development of a Reference Measurement System for sustainable PT/INR Standardization)**

Chair : Prof. Christa Cobbaert (NL)

- Collaboration with ISTH (International Society on Thrombosis and Haemostasis)
- To **develop a harmonized reference measurement procedure** based on the WHO manual tilt tube technique as well as the complete reference measurement system for **global standardization** of the PT/INR test.
- Establishment of one WHO International Standard for thromboplastin, replacing the current system in which two International Standards are coexisting.
- To **establish a network of calibration labs** and of WHO reference laboratories

Working Groups : New Projects

- **Working group on Brain Natriuretic peptides (WG-BNP)** Chair : M. Quaglia (UK)
 - Standardization of 1-32 BNP and NT-Pro-BNP
 - Obvious clinical needs in cardiology and emergency medicine
 - Association of all stakeholders including manufacturers and clinicians
- **Working group on Extracellular vesicles**
 - **“Extracellular vesicles”** (EVs; term includes exosomes, microvesicles, microparticles, etc.), small cell-derived submicron particles abundantly present in all body fluids and thought to contain clinically relevant information.
 - Cell-type specific EVs are measured in body fluids by flow cytometry (detailed information at a rate of thousands particles/s), often as potential biomarkers of disease.
 - Ask support for educational goals and visibility at IFCC meetings.
 - EB advices to collaborate with IFCC EMD
- **Working group on neonatal bilirubin standardization**
 - Clinical context : severe neonatal hyperbilirubinemia

REVIEW ARTICLE

Diagnostic methods for neonatal hyperbilirubinemia: benefits, limitations, requirements, and novel developments

Christian V. Hulzebos¹, Libor Vitek², Carlos D. Coda Zabetta³, Aleš Dvořák², Paul Schenk⁴, Eline A. E. van der Hagen^{5,6}, Christa Cobbaert⁴ and Claudio Tiribelli⁷

Pediatric Research (2021) 90:277–283; <https://doi.org/10.1038/s41390-021-01546-y>

Impact: Manufacturers should make TSB test results traceable to the internationally endorsed total bilirubin reference measurement system and should ensure permissible limits of measurement uncertainty.

- Possible collaboration with IFCC ETD

To standardize (or to harmonize)

- **Many important accomplishments of SD** : a lot of assays have been standardized (or harmonized) in the last decades
 - ✓ Simple parameters : glucose, creatinine, cholesterol
 - ✓ Enzymes
 - ✓ Peptides, hormones, proteins :
 - TSH (IFCC-C-STFT)
 - FT4 (IFCC-C-STFT)
 - CDT (IFCC-WG-CDT)

But the number of medical tests requiring standardization or harmonization remains enormous !

- **New challenges** :
 - Huge number of tests to standardize
 - New concepts = molecular definition of diseases
 - More focussing on clinical needs / contexts
- **IFCC = Scientific expertise**
 - « Catalist »
 - « Conductor » (P. Gillery, CCA 2021)
- **Common vision IFCC and partners**
 - NMIs
 - Manufacturers
 - ICHCLR / JCTLM

IFCC and other stakeholders of standardization

Editorial

Clinical Chimica Acta (2021) 184-186



- Clinicians
- Clinical scientific societies



- IFCC
- National metrology institutes
- Reference laboratories
- Academic laboratories
- Clinical laboratories



- Patients
- Patient associations



- Manufacturers
- EQA providers

- Ministries
- Health regulators and agencies



SD - Interactions of IFCC with NMIs and the “metrology world”

- IFCC-SD believes that a **global approach** is necessary involving :
 - Closer participation with partners directly involved in standardization (BIPM, NMIs, WHO)
 - Regulators
 - Professional / Scientific Societies and Academies
 - Individual Laboratory Professionals
- **Significant actions of SD in Metrology over the last years :**
 - More systematic reciprocal involvement of NMIs and IFCC-SD in review / management of projects
 - **MoU signed between IFCC and BIPM in 2020**
 - Involvement of NMIs in IFCC Cs / WGs (WG-PCT chaired by a NMI scientist)
 - Association of IFCC-SD members to TraceMedLab Project
 - Participation of SD in CCQM / CCU meetings
 - Participation of SD representative in CCQM WGs (*eg* PAWG (working group on Protein analysis))
 - Participation of SD in Metrology events

Communication in Metrology

Happy World Metrology Day 2021!

The Joint Committee for Traceability in Laboratory Medicine (JCTLM) is celebrating World Metrology Day on 20 May 2021. The theme this year is "Measurement for Health".

Watch the videos on measurements in Laboratory Medicine for broader perspectives on the importance of metrological traceability in laboratory medicine for individual patients and for risk assessments in populations.

What is Laboratory Medicine?

Greg Miller, PhD, Chair, JCTLM
Professor of Pathology, Virginia Commonwealth University Health System, USA

What happens in your local laboratory?

Graham Jones, Department of Chemical Pathology, St Vincent's Hospital, Sydney, Australia

Tools for obtaining laboratory result comparability: What the JCTLM is offering?

Mauro Panteghini, Centre for Metrological Traceability in Laboratory Medicine (CIRME), University of Milan, Italy

What is special for measurements in Laboratory Medicine?

Elvar Theodorsson, Linköping University, Sweden

Chem-Bio Metrology for Laboratory Medicine

Sang-Ryoul Park, CIPM/CCQM
Korea Research Institute of Standards and Science

How IFCC Improves the standardization of results in Laboratory Medicine

Prof. Philippe Gillery, MD, PhD, IFCC-SD Chair
Professor of Biochemistry and Molecular Biology, Faculty of Medicine and University Hospital of Reims, France

Platelet Counting Standardization

Paul Harrison, BSc, PhD, FRCPath, ICSh board member
Associate Professor, Institute of Inflammation and Ageing, University of Birmingham, UK

How to achieve traceable measurements in Laboratory Medicine jointly in Europe: The European Metrology Network for Traceability in Laboratory Medicine

Bernd Güttler and Rainer Stosch, PTB, Germany

World Metrology Day



Measurement for Health



20 May 2021

www.worldmetrologyday.org

EMN TraceLabMed & TC for Metrology in Chemistry Stakeholder Workshops on Measurement Challenges



10 November 2021, UTC+1

10:00 Welcome & Introduction

10:15 EURAMET MSU

Funding Programme: Timeline, Budget, Call Scope

10:30 Stakeholders' perspectives:

10:30 Prof. Philippe Gillery – Faculty of Medicine Reims University & IFCC-SD
"Need for Metrology to Support Standardisation Activities of the IFCC Scientific Division"

15:00 Wrap up & Discussion

16:00 End

EUROPEAN
METROLOGY
NETWORKS



4 | 10 November 2021
Pandemics | Laboratory Medicine

A unified workshop



JCTLM Members and Stakeholders biennial meeting and workshop

Overcoming challenges to global standardization of clinical laboratory testing: reference materials and regulations

A workshop organized by the IFCC Scientific Division, the International Consortium for Harmonization of Clinical Laboratory Results (ICHCLR) and the Joint Committee for Traceability in Laboratory Medicine (JCTLM)

Dates: 6-10 December 2021
Location: Virtual sessions
Format: Two 2-hour discussion sessions on three separate topics with a final combined session to develop workshop recommendations
Workshop goals:
The workshop will develop and publish recommendations how the laboratory medicine community can address challenges related to reference materials and to country and region specific regulations to more effectively achieve standardized results on a global basis.
Organizing committee: Philippe Gillery, Christa Cobbaert, Greg Miller, Gary Myers, Joe Passarelli, Robert Wielgosz, Ian Young, Elvar Theodorsson



JCTLM Members and Stakeholders biennial meeting and workshop

Overcoming challenges to global standardization of clinical laboratory testing: reference materials and regulations

Session 1: What are the needs and logistical challenges for standardized results?

Session 2: What are the challenges for CRM producers?

Session 3: What are the challenges to meet regulatory requirements in different countries or regions?

Session 4: Develop workshop recommendations for publication and follow up actions

<https://www.bipm.org/en/committees/jc/jctlm/wg/jctlm/2021-12-06>

- Major concern of regulations around the world
- Outcome : manuscript with recommendations (currently in progress)

- High level of publications (see website)
- 2021 = SD-Managed CCA Special issue

Clinica Chimica Acta 522 (2021) 184–186



Contents lists available at [ScienceDirect](#)

Clinica Chimica Acta

journal homepage: www.elsevier.com/locate/cca



Editorial

IFCC Scientific Division: A conductor of standardization in laboratory medicine



Editor

Philippe Gillery, MD, PhD
SD Division Chair

⇒ **10 manuscripts written by Cs - WGs**

Changing landscape

- **COVID pandemic and upcoming stringent Regulations on IVD-manufacturers & lab professionals (IVDR, REACH,...) cripple the IFCC SD efficiency through**
 - unharmonized regulatory requirements: Chinese regulations >> EU IVDR > USA FDA ... are a big burden for IVD-manufacturers
 - deprioritization of test (re)standardization
 - increased costs and disruptive for innovation
- Limited uptake of new RMs, RMPs, RMS in the past 2 years**

Changing landscape

- **What hinders adoption / implementation of (re)standardized tests?**
(concerns of several Cs/WGs *e.g.* : C-HAT, C-STFT, WG-PCT)

Appraisal of currently functioning IFCC SD :

- Good will approach with mostly volunteers
- No predefined criteria for IFCC endorsement of RMs/RMPs/RMSs, in contrast to those for JCTLM endorsement
- No predefined competences of IFCC WG/C chairs and members on metrology and standardization
- Every WG/C finds out the wheel
- General lack of education on metrological traceability and test standardization
- Value assigned, commutable Reference Materials are unavailable early in the test development process
- Limited financial budget

Changed landscape

- **How to improve adoption effectiveness of (re)standardization projects?**
 - Guidance for WGs/Cs to reach IFCC endorsement/ JCTLM approval
 - Regulators / notified bodies at the table as these are essential for market access of tests
 - Successful adoption/implementation of RMS demands effective governance in tight network organizations/ consortia with clearly defined roles of all stakeholders, including clinical societies
 - Common goals and non-overlap of activities among all partners. Quest for one shared vision with unique activities, alignment and transparency!

The challenges for the future...

Clin Chem Lab Med 2018; 56(10): 1598–1602

DE GRUYTER

Opinion Paper

Christa Cobbaert*, Nico Smit and Philippe Gillery

Metrological traceability and harmonization of medical tests: a quantum leap forward is needed to keep pace with globalization and stringent IVD-regulations in the 21st century!

<https://doi.org/10.1515/cclm-2018-0343>

Received April 4, 2018; accepted April 5, 2018; previously published online May 7, 2018



General Conference in Brussels, October 2022



IFCC

International Federation
of Clinical Chemistry
and Laboratory Medicine

SD Report to IFCC Council



C.M. Cobbaert, Vice-Chair



P. Gillery, Chair



Thank you !



April 10th, 2022

Twenty Forth Triennial meeting of Council

ifcc.org