

68th Meeting
SCIENTIFIC DIVISION
Minutes
Conference Call – December 22nd, 2021
and January 12th, 2022,

Members:		Abbr.	Term and Time of Office	
Philippe GILLERY (FR)	Chair	PG	2 nd	2020 01 - 2022 12
Christa COBBAERT (NL)	Vice-Chair	CC	2 nd	2020 01 - 2022 12
Garry JOHN (UK)	Secretary	GJ	1 st	2021 03 - 2023 12
Barnali Das (IN)	Member	BD	2 nd	2021 01 - 2023 12
Konstantinos MAKRIS (GR)	Member	KM	2 nd	2020 01 - 2022 12
Mario PLEBANI (IT)	Member	MP	2 nd	2020 01 - 2022 12
Michael ROTTMANN (DE)	Corporate Rep.	MR	1 st	2020 03 - 2022 12
Karen PHINNEY (US)	NIST Rep.	KP		
Liesbet DEPREZ (BE)	JRC Observer	LD		
Ian YOUNG (UK)	ICHCLR Observer	IY		
Chris BURNS (UK)	NIBSC Consultant	CB		
Greg MILLER (US)	JCTLM Chair/SD Cons.	GM		
Yang ZHEN (CN)	NIFDC Rep.	YZ		

EXECUTIVE SUMMARY - SCIENTIFIC DIVISION 68th MEETING

Conference Call – December 22nd 2021

Present: Philippe Gillery (Chair), Christa Cobbaert (Vice-Chair), Garry John (Secretary), Barnali Das, Michael Rottmann (Corporate Representative, Greg Miller (JCTLM Chair/SD Consultant), Liesbet Deprez (JRC Observer), Karen Phinney (NIST Consultant [joined at 15.10h]), Ian Young (SD Consultant/ICHCLR Observer [joined at 15.43h]).

Apologies received from: Konstantinos Makris, Mario Plebani, Chris Burns (NIBSC Consultant), Yang Zhen (NIFDC Observer).

Conference Call – January 12th 2022

Present: Philippe Gillery (Chair), Christa Cobbaert (Vice-Chair), Garry John (Secretary), Konstantinos Makris (Members), Michael Rottmann (Corporate Representative), Karen Phinney (NIST Consultant), Ian Young (SD Consultant/ICHCLR Observer), Greg Miller (JCTLM Chair/SD Consultant), Chris Burns (NIBSC Consultant), Liesbet Deprez (JRC Observer), Ralf Josephs (BIPM Observer), Barnali Das (joined 14.00h) Mario Plebani, (joined towards the end of the meeting). Gunnar Nordin and Young Bae Hansen joined for discussion on VIM4

Apologies received from: Yang Zhen (NIFDC Observer),

PG welcomed Ralf Joseph /BIPM Observer as new member

All documents/reports submitted prior to the SD-EC Meeting are in Appendix 1 that can be read on request

2. APPROVAL OF MINUTES

Appendix 1

The minutes of the 67th SD meeting were approved as written with no changes.

Executive Summary for IFCC web site approved with no changes

Action items following 67th SD Meeting are listed in the Executive Action Log (**Appendix 2**)

Actions Complete:

KM to forward documents from CCQM relating to HbA1c to GJ and Dr Emma English. KM forwarded documents, a date to meet will be organised

PG will ask for more information on relationship between C-RIDL and new IFCC Taskforce on Global Reference Intervals. PG has had an email discussion with the chair of the committee she is liaising with the new TF; the two working parties are complimentary and have clear defined roles.

BD has had no communication from the Chair of PAPP. There has been no response and BD was wondering if email address is correct. PB will check email address. BD reported that the email address is correct.

CC stressed her concern over the ongoing issue related to resources available to accomplish many of WG-SIA tasks. GM stated that Michael Steffes probably sees this as a research activity rather than standardization imitative. CC to follow up the discussion with Michael Steffes. CC suggested that this can be discussed at WG level.

5. CHAIRMAN'S REPORT

In important issue was to reinforce the relationship between SD and partners involved in metrology and we welcome a representative from the BIPM also trying to participate in metrological WGs particularly Protein Analysis WG. Reflections over the actions and projects of the SD have been initiated, discussions with CC focused on better defining the goals of the SD and give rules to working parties in order to better achieve their goals; PG reminded the committee that this is his last year as chairmen of SD and CC will take on the role at the end of 2022, and it is important to have clear vision over the transition period. CC commented that it is increasingly important to look at the Metrological needs to ensure accurate results and hopes to build on the good work already done with colleagues in the Metrology world. Will need how best to work together and set realistic timelines, working together over standardisation will improve things globally. These are challenging times and we need to expand MOU with relevant organisations.

5.4 European Federation of Clinical Chemistry and Laboratory Medicine (EFLM)

The EFLM TF has been trying to find out what the current situation is. It is obvious that the amount of work required has been grossly underestimated. There are about 40,000 medical tests that need consideration. There is a risk based classification, but all tests have to go through the EU Regulatory procedure; scientific validity has to be documented depending on the intended use of the test, but in addition analytical quality has to be defined in terms of accuracy and sustainability. Following the work of the TF the EU now recognise the amount of work and the unreadiness of manufacturers due to the amount of work required. Legislation has not changed, but now there is a phased rollout for both commercial and in-house tests (more time to decide whether to continue or not). Specialist low volume tests need special consideration. There is now postponement until

2024 – 2028 depending on the risk; in-house tests will be the later date. Manufacturers have been working on these new requirements for the last two years.

6. INTERNATIONAL ORGANISATIONS

6.1 WORLD HEALTH ORGANISATION (WHO)

PG has received no communication regarding IFCC attendance at the WHO expert committees.

ACTION: CB will continue to follow this up.

6.22.1 Joint Committee on Traceability in Laboratory Medicine (JCTLM)

1. General observations

- Effectiveness of test results for patient care is the primary goal for standardization and the guiding principle for optimized practices supporting standardization.
- Before starting a standardization project for a measurand, an assessment should be performed to determine the clinical impact of the current situation, and of the resources and total cost to complete standardization.
- Educational curricula for providers, laboratorians, IVD producers and regulators are needed to improve understanding of the standardization process and its value to promote safe and effective clinical laboratory tests.

2. Fit-for purpose matrix-based certified reference materials

- Definition of the measurand and the molecular structure actually measured by IVD devices is important.
- IVD manufacturers need an assured supply of a CRM with a backup supplier; excessive redundancy of suppliers is not the best use of limited resources.
- Prioritization of measurands for which new CRMs are needed should involve clinical laboratories, clinical practice groups, IVD manufacturers, NMIs and other producers.
- Commutability of matrix-based CRMs with clinical samples is an essential property that consumes a substantial fraction of the resources.
- Listing RMs known not to be commutable would be useful.
- Agreeing on a standard content and format for a CRM certificate or report would aid IVD manufacturers with regulatory submission documentation.

3. Meeting regulatory requirements in different countries

- Regulatory agencies promote safe and effective patient care. Regulations and requirements for data submission are different among regulatory agencies.
- Cost for regulatory submissions in multiple countries has made IVD manufacturers reluctant to adopt some newly developed standardization initiatives.
- Regulators promote a risk based assessment to determine how much new data is needed to review, on a case by case basis, the impact of recalibration. Standardized

results promote reduced risk for erroneous medical decisions and should be part of the risk assessment.

- Agreeing on requirements for documentation when a calibration hierarchy is modified to achieve standardized results for clinical samples, and no other changes are made to an IVD device would make regulatory submission simpler.
- Including representatives from regulatory bodies along with clinical laboratories, clinical providers, RM producers and IVD manufacturers in standardization projects will help to clarify data requirements for regulatory submission that can be collected as part of the standardization activity.

Cooperation and collaboration among all stakeholders is essential to optimize standardization of clinical laboratory results in the best interests of the patients we all serve.

4. Next steps:

- The organizing committee will prepare a manuscript with conference observations and recommendations.
- The manuscript will be posted to the JCTLM web site as a Google document for comment. Participants will be notified when posted.
- The final version will be submitted for publication.

JCTLM will roll out a new web site in April/May 2022. JCTLM recognises there is a need for training to submit to the website; educational material will be made available. Uncertainty data is probably one of the more difficult aspects in getting JCTLM approval in relation to ISO regulations. CC commented it is unclear how you move from IFCC endorsed to JCTLM acceptance, she supported the need for training. GM emphasised it is important for IFCC WG to look at JCTLM documents in the early stages of their planning to ensure the validation experiments comply with requirements for submission. GM proposed that IFCC and JCTLM should collaborate to produce guidance documents.

ACTION: PG to revisit IFCC and JCTLM collaboration to produce guidance on this in coming meetings to monitor progress

6.22.2 Joint Committee for Guide in Metrology (JCGM)

Gunnar Nordin and Young Bae Hansen joined the meeting for this item. PG explained that there is an ongoing process of VIM revision. And there is discussion started by JCGM WG2 where Gunnar is the IFCC representative. PG stated strongly that IFCC must be fully involved in discussions.

Gunnar spoke to the presentation below which differs from that circulated prior to the meeting and shown in Appendix 1.



Microsoft PowerPoint
97-2003 Presentation

GN: There are 8 organisations in JCGM; which share the responsibility for the VIM. GN is on the group due to his involvement with CNPU, and appointed IFCC representative.

VIM3 is a document in three sections. Devices for measurement, Measurement and Quantities and units In VIM4 these three sections are now arranged into six sections; the Measurement sections

have been kept; the Devices for measurement chapter has been divided into three. And a sixth chapter added on Nominal Quantities. The new document was sent out for comment to JCGM stakeholders and 1500 comments were received most comments were to the new chapters.

There are three types of “observation” in VIM. There is no name for “ratio quantity” (see presentation). A substance concentration cannot have a value unless it is related to something. Quantity is not defined.

There is an argument that VIM should only cover measurements with values and units; but some think all should be covered; there is no right answer. GN asked for support from IFCC to include all types of investigations in future VIM.

What should an “observation” be called? In ISO 15189 “examination” covers all three types of observations. But this was not accepted by the WG so in VIM4 this is restricted to the third type of observation. Theoretically “measurement” or “examination” could apply to all three types of procedures. GN asked for opinions as to which should be recommended.

GM asked for discussion during the presentation:

What is a quantity? Both GM and IY support GN suggestions as he is the expert. CC is keen to keep the link to ISO 15189.

GN argued for the term “examination” but the arguments against is that the term may be thought to relate to examination (as in written examination). Another term being considered is “evaluation”. Examination is recognised by ISO 15189. GM prefers the term “measurement” but any will be acceptable as long as we are consistent.

What is a value? One option is as an individual quantity, but there are strong objections to this. GN argues strongly that value is a quantity. This is the historical position of IFCC. GM agrees that we should be consistent across all measurements and examinations.

KM queried that a quantity is something that is accompanied by units. GN stated that is one view, but there is no specific term

The last point is the controversial question of what is “accuracy”? Vim refers to three different accuracies: accuracy of measurements, accuracy of results and accuracy of instruments. VIM4 has retained that generic definition of accuracy. But the definition has changed from comparing to a “true quantity value” to comparing to a “reference value”; so the accuracy can be known if the reference value is known; this is controversial. GM asked is accuracy the same as bias? As stated this can be considered bias. The next version on VIM should be clear on accuracy and bias. GM also stated that some of the ISO documents state that accuracy of an individual measurement includes bias and imprecision components, but this has always been unclear. KM asked how do you differentiate between the accuracy of a method and the accuracy of a result? GM stated this will depend on the context.

What is “uncertainty”? Can this be expressed mathematically? VIM\$ keeps the view that uncertainty is something that can be expressed mathematically. IY strongly supports that uncertainty is something that can be expressed mathematically/

PG asked if GN can send a questionnaire that is intended to be sent to the societies. GN stated that a questionnaire is not decided on yet.

ACTION: PG to work with GN to organise a questionnaire.

Young Bae Hansen stressed that it is very important that the VIM is developed. YH commented that they are trying to be engaged with ISO TC215 trying to have discussions about measurement units and properties. NPU codes are not currently being used optimally; trying to look at what kind of information is needed to make reports comparable.

6.22.3 BIPM Consultative Committees (K. Makris)

6.22.3.1 Consultative Committee for Amount of Substance – Metrology in Chemistry (CCQM)

KM updated the committee on the CCQM Working Group on Protein Analysis (PAWG). CC stated that Natriuretic peptides plus TnI and Apolipoprotein standardisation is covered by the Cardio Met project; CC is involved in this project and they are very keen to work with IFCC.

6.22.3.2 CC for Units (CCU)

Appendix 1

No specific comments.

6.23. International Standards Organization (ISO)

Discussion between YH and IY; it was agreed that YH would represent SD in this WG.

GM stated that ISO TC212 WG 2 is currently revising 15193 and 15194 on reference measurement procedures and reference materials; there are a number of SD members involved. This is important as JCTLM will have to revise submission process based on new ISO requirements. This should be a common goal; IY will represent SD.

RJ is on revision team for 15193 there is progress on line, now 70-80% through the standard.

6.31 JOINT RESEARCH CENTER (JRC)

Appendix 1

CRMs for auto immune disorders [IFCC Committee on Harmonization of Autoimmune Tests (C-HAT)]

CRM for IgG anti-B2GP (antiphospholipid syndrome (APS)): ERM-DA477/IFCC. Report of the WHO drafted, still on track to submit the WHO as a candidate for the international standard in Spring 2022. If accepted the WHO will assign the arbitrary values. NIBSC has agreed to act as mediator and custodian of a part of the batch. JRC will take care of the distribution of the CRM to IVD manufacturers and clinical laboratories.

CRM for IgG and IgA anti tissue transglutaminase (anti-tTG) (Coeliac disease): EURM-487/IFCC
The material has been processed. Homogeneity and stability studies planned for Jan 2022.

IgG anti-GBM (vasculitis): ERM-DA484/IFCC

Draft paper on the commutability study of the pilot batches prepared. Most suitable starting material was selected. Purchase of the large batch ongoing.

CRMs for CSF proteins [IFCC Working Group on CSF proteins (WG-CSF)]

CRM for A β 1-40 in CSF: ERM-DA480/IFCC, ERM-DA481/IFCC, ERM-DA482/IFCC

Studies to evaluate if the existing CRMs (ERM-DA480/IFCC, ERM-DA481/IFCC and ERM-DA482/IFCC) can also be certified for A β 1-40 are ongoing. Homogeneity, short and long-term stability have been tested and results are good.

A calibrant peptide has been selected and quantified with amino acid analysis (AAA) by LNE, LGC and JRC. Purity assessment is still ongoing in collaboration with LNE and LGC. The impurities have been identified, the final value assignment for beginning 2022.

Development of CRM for Tau and Neurofilament light (Nfl): on hold until new contract agent recruited, planned for Spring 2022.

CRMs for Haemoglobin A2 [IFCC Working Group on Standardisation of Haemoglobin A2 (WG-HbA2)]: ERM-DA485/IFCC and ERM-DA486/IFCC

For the matrix CRM: 2 lyophilised materials have been processed: 1 with normal HbA2 levels and 2 with elevated HbA2 levels. First checks with several commercial assays show good results. Homogeneity and short term stability studies planned for January 2022.

CRMs for apolipoproteins [IFCC Working Group on apolipoproteins by Mass Spectrometry (WG-APO MS)]

For the peptide calibrators for Lp(A): The JRC has produced the first batches of peptides calibrators that can be used to investigate the completeness of the digestion of apo(a) in the candidate RMP. The purity check and AAA measurement on the peptides calibrators will be done by the JRC and LNE.

For the serum CRM for Lp(a): several candidate RMs have been investigated in a commutability study. Results of this study indicate that CRM based on unspiked pools of human serums have the best commutability profile. Publication on the correlation/commutability study is prepared and submitted to the IFCC SD for review.

Work on standardisation/harmonization faecal immunochemical testing [IFCC working group in Faecal Immunochemical Testing (WG-FIT)]

The results of the correlation/commutability study are analysed. The results of 4 frequently used FIT methods correlated quite well but there is a significant bias. So using a common threshold for these 4 methods is currently not feasible. The 7 candidate RM were tested for their commutability and 2 of them had a good commutability profile. These 2 RM consist of Hb from human blood diluted in the specific buffers of each FIT method. Addition feasibility studies are needed to test if these RM can be produced in larger stable batches. The value assignment will also be difficult given the low Hb concentration: 1000 times lower than in blood.

CRMs for enzymes [IFCC working Group on Pancreatic Enzymes (WG-PE)]

The project for the production of a CRM for the catalytic activity of alkaline phosphatase (ALP) is started.

The CRM for the catalytic activity of aspartate aminotransferase (AST) will need to be replaced within 3 years so the search for suitable starting material has started.

CRM for Oestradiol in human serum

The sales stocks of the CRMs BCR-576-578 are running low. These materials will be replaced with new batches which will be tested for their commutability for several IVD methods. Discussions ongoing to include these new materials in the upcoming CCQM study on oestradiol in 2024-2025.

LD commented that for HbA2 in early 2022 there will be data on stability and homogeneity. In spring there will be materials to be shipped to laboratories to do the reference measurement procedures; results hopefully by Summer. Material may be available by the end of 2022. This will be a lyophilised material, commutability is being checked, but no problem found to date.

6.33 NATIONAL INSTITUTE OF BIOLOGICAL STANDARDS AND CONTROL (NIBSC)

CB commented that NIBSC continues to produce the reference material to support the global response to the pandemic; includes Ab standards, increasingly Ag standards and also vaccine testing and release both for the UK and now COVAX and the WHO response. However many work programmes are now back up and running.

New International Standards projects endorsed

Proposed 2nd WHO International Standard for AFP, human cord serum

Proposed WHO 1st International Standard for anti-thyroglobulin

Proposed WHO 5th IS for Hepatitis B Virus DNA for Nucleic Acid Amplification Techniques

Proposed WHO Reference Panel for antibodies for SARS-CoV-2 Variants of concern

Proposed WHO 2nd International Standard for anti SARS-CoV-2 immunoglobulin

Proposed 1st WHO International Standard for SARS-CoV-2 Antigen

Additional activities of note

Covid19

Support to the diagnostic pillar of the ACT Accelerator will be provided through the proposed development of the SARS-CoV-2 antigen standard for rapid diagnostic testing (see above).

NIBSC will organise a collaborative study in late 2021 and early 2022 with the aim of submitting a proposal to the ECBS for the establishment of the standard in October 2022.

The recently established First WHO International Standard for anti-SARS-CoV-2 immunoglobulin has been widely adopted and this has resulted in its depletion within 8 months. NIBSC will now develop a replacement standard, although there is a recognised challenge of sourcing a suitable replacement material. In addition, NIBSC will develop a panel of reference sera specific for SARS-CoV-2 variants of concern that could be expanded should new variants emerge. The panel will facilitate development of the essential serological assays needed to study the impact of new variants on the efficacy of existing vaccines and therapeutics.

4th WHO IS for pituitary TSH

The collaborative project with the Committee for the Standardisation of Thyroid Function Tests (C-STFT) described last time, continues to progress well with sample collection for the replacement C-STFT panel ongoing.

The 1st WHO International Standard for anti- β 2GPI Immunoglobulin G in human serum

Immunoglobulin G autoantibodies against β 2GPI are used in the diagnosis of antiphospholipid syndrome (APS), according to an international consensus statement on the classification criteria for definite APS. In APS, patients are at higher risk of thrombosis and pregnancy complications. These autoantibodies are also present in up to 40% of patients with systemic lupus erythematosus. The clinical community has highlighted the unacceptable variability in anti- β 2GPI measurements, which derives mainly from differences in the immunometric methods, calibration procedures and the lack of a suitable reference material. NIBSC is working with the JRC to characterize and evaluate a candidate reference material.

European Metrology Network on Traceability in Laboratory Medicine – TraceLabMed

NIBSC continues to be a member and participated in two important workshops organised by EURAMET's European Metrology Network on Traceability in Laboratory Medicine (EMN TraceLabMed) and the Technical Committee for Metrology in Chemistry (TC-MC).

Open workshop on measurement challenges – laboratory medicine

Open workshop on measurement challenges – SARS-CoV2 and future pandemics

6.37 NATIONAL INSTITUTE OF STANDARDS AND TECHNOLOGY (NIST)

Appendix 1

6.38 The International Consortium for Harmonization of Clinical Laboratory Results (ICHCLR)–

With regard to IFCC the Council of ICHCLR has approved an advertisement for applications to carry out work on high priority measurands on the ICHCLR database; advert will go out early January. Intention is to propose applicants to set up a WG; need to agree a reporting mechanism, preference from ICHCLR Council is that the WG would report in through ICHCLR and the chair of ICHCLR would report back as an annual or six monthly report to SD. This has not been discussed and is not the original structure but is the one preferred by Sverre Sandberg and Council; IY believes this will not make a big difference in practice but will mean but rather than being IFCC WGs they will be ICHCLR WGs. PG asked how will these WGs be formed? IY thinks ICHCLR Council supports a dual reporting line to SD and ICHCLR. The WGs will have a program of work for three years, if possible to carry out full metrological standardisation in that period that would be the preferred approach, but more likely the approach will be to achieve comparability of results probably not through a mechanism rather than full metrological standardisation

6.50 ILAC

Nothing to report.

8.2 COMMITTEES

PB stated that membership and the chair of several committees will need reviewing due to incumbents reaching the full term of their appointments. As the SD was not able to meet PG has submitted some renewals of member and chairs to the EB in order to save time and to be able to renew for 2022.

8.2.6 C-NOMENCLATURE, PROPERTIES AND UNITS (C-NPU) - Appendix 1

Program Manager: IY

K. Furuta Member proposed for 2nd term, this has received EB approval.

8.2.11 C-MOLECULAR DIAGNOSTICS (C-MD)

Program Manager: PG

No update from the chair. One member is at the end of their first term, chair recommended membership should not be renewed. PG commented that in a message from EB suggested that the activity of this committee be reviewed. PB confirmed this was the message but not sure as to what was meant, this needs clarification.

ACTION: PG to ask the EB to clarify this message, and will ask the chair to provide an update so SD can make decisions.

ACTION: PB to prepare document for new member.

ACTION: PG (January): will ask the chair to revise the ToR and current projects to decide on the future of the committee

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

Program. Manager: CC

M. Pérez-Urquiza and T. Badrick Members proposed for 2nd term, pending EB approval. There are no issues from A. Kessler about renewal of these members.

List 2021 accomplishments Term of Reference 1

The chair of C-TLM participated in the (virtual) annual meeting of JCTLM DatabaseWG and JCTLM Executive Board. The results of the annual survey RELA for calibration laboratories are discussed and were among other factors responsible for the decision of listing nominated calibration laboratories in the JCTLM DataBase.

List planned activities in 2022 for Term of Reference 1

C-TLM will contribute to the next JCTLM symposium "Traceability in laboratory medicine - vital for clinical value" at WorldLab2022 in Seoul which was postponed to June 2022. The title of the lecture will be "Traceability for Laboratory Medicine – the role of the national measurement institute" and will highlight the qualification of calibration laboratories and their impact on implementation of metrological traceability.

List 2021 accomplishments for Term of Reference 2

578 results of RELA 2021 were published in September (<http://www.dgkl-rfb.de:81>). C-TLM as advisory board of this IFCC survey has been discussed the results in detail at the annual meeting. The results were presented at the JCTLM Members & Stakeholders On-line Meeting on December 13, 2021. The revision of the RELA procedure manual has been started and will be proceed in 2022. One subject of the revision is the discussion whether the limits of equivalence are adequate or have to be changed.

List planned activities in 2022 Term of Reference 2

For RELA 743 orders (+8%) are registered, the dispatch of the samples is in progress. The evaluation will be published in June 2022.

Special focus will be on HbA1c. C-TLM organizes a joint project with C-EUDB and CCQM. The participants of RELA 2022 and 9 metrology institutes will analyse the same samples within the separate projects. After the deadline all results can be compare to each other. At the same time, the participants of RELA 2022 will get two additional lyophilized samples. These samples are prepared for the EurA1c study 2021. Similar to the comparison between RELA and CCQM, the results of the calibration laboratories participating in RELA2022 can be compare to those of the routine labs participating in the international survey EurA1c2021. Finally, we will demonstrate the current status of traceability between approx. 5000 routine labs, 20 calibration labs and candidates labs respectively, and 9 metrology institutes.

List 2021 accomplishments for Term of Reference 3

Report HbA1c Network

Carla Siebelder, Network Coordinator, Eline van der Hagen, associate Network Coordinator

As IFCC HbA1c Network two intercomparison studies are organised annually. However, in 2021 the collection of blood and therefore the study had to be postponed due to the COVID19 pandemic. For the study about 60 diabetic volunteers, vulnerable patients, are required to donate blood and it was unethical and also legally restricted to let them donate in the beginning of the year, in the heat of the pandemic. We were lucky to be able to organise the campaign in July, where most people were vaccinated. As a result there was only one study this year. The approved network laboratories, candidate laboratories (Brazil and India) and the designated comparison method networks in the US and Japan participated. Due to the pandemic it was a challenge to get the samples shipped over the world.

The study is finished. All approved network laboratories kept their approval and the master equations between the IFCC RMP and the designated comparison methods were again confirmed. The 2 candidate laboratories didn't gain approval. We have 19 approved network laboratories. Due to the postponement of EuroMedLab Munich the face-to-face meeting scheduled on 1 December is cancelled and the network will have a Zoom meeting instead.

For educational activities the network is part of the IFCC C-EUDB. Due to COVID there haven't been live congresses but some members gave Zoom lectures. In 2022 a symposium is scheduled at the IFCC WorldLab in Seoul.

EurA1c, the multinational project in which national EQA organisers share two samples, was organised for the fifth time in 2020. We have seen a yearly increase in participation. In 2020 we had 27 EQA organisers from 22 countries participating. The number of participating laboratories was more than 5000. Currently the 2021 trial is running.

Report CDT Network

Carla Siebelder, Network Coordinator, Eline van der Hagen, associate Network Coordinator

The CDT network of reference laboratories organises an intercomparison study annually. In 2021 all 5 approved network laboratories and 1 candidate laboratory participated. A second candidate lab was not yet ready to participate. All approved labs kept their status of approval. The candidate was approved for the first time. According to the rules of the network this candidate has to pass in next year's study (two consecutive studies) to get the status of approved lab.

The network intended to meet at EuroMedLab Munich on Sunday 27 November but due to the postponement of the congress a Zoom meeting was held instead where the annual intercomparison study was discussed.

List planned activities in 2022 for Term of Reference 3

The CDT network of reference laboratories organises an intercomparison study annually. Expansion of the network by recruitment of new reference laboratories was also discussed. Focus

of the WG continues to be on global implementation of standardised results and promotion of the CDT test.

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

Program. Manager: BD

There is no update for this committee

Yesim Ozarda has reached the end of her term and has suggested Thomas Streicher as a replacement; this suggestion followed a discussion with PG. This suggestion was put to the EB who accepted this nomination. PG suggested we acknowledge the good work done by Yesim as there were many difficulties, and asked if Paola could prepare a letter of thanks.

There needs to be a call for nominations for 2 member positions to be open (substituting Y. Özarda and D. Kang)

ACTION: PB to prepare a letter of thanks.

ACTION: Place call to member societies for 2 nominations

8.2.25 C-STANDARDIZATION OF THYROID FUNCTIONS TESTS (C-STFT)

Program. Manager: BD

List 2021 accomplishments for Term of Reference 1

A1: Maintaining the reference system for fT4:

A network of reference laboratories was established and an interlaboratory comparison study among network laboratories was successfully conducted. Laboratories meet requirements for reference measurement procedures and are traceable according to ISO 17511:2020. Most of these laboratories are now active providing reference measurements to national standardization efforts, EQA providers and manufacturers. The reference laboratories are located at: Ref4U (Belgium), CDC Clinical Reference Laboratories (USA), Radboud University Medical Center of Nijmegen (The Netherlands), and Reference Material Institute for Clinical Chemistry Standards (Japan).

The Network collaborated with the NIST (USA) to characterize serum-based materials.

A2: Maintaining the reference system for TSH:

The study design to create and characterize the next TSH harmonization panel according to ISO 21151 was completed, Ethics approval at UGhent was obtained, and Material Transfer Agreements for collecting and processing sera are in place. Specimen collection is initiated in Belgium, Croatia, Japan, Norway and Belgium.

TSH harmonization based on the IFCC C-STFT reference system is, as of this year, officially implemented in Japan and assay manufacturers are now using the harmonization panel to adjust assay calibration, as stated in a publication by one manufacturer.

Established collaboration with NIBSC to characterize new TSH reference material to maintain the IU system. Characterization will be conducted together with the characterization of the new TSH harmonization panel.

A3: Successfully completed a 36 months stability study for serum-based reference materials for fT4 and TSH that is based on single-donor patient samples. CDC (USA) collaborated on the statistical analysis. No analyte degradation was identified. Data suggest that slight sample concentration may occur and alternate storage containers are now being explored. The

B1: CDC Clinical Standardization Programs launched in 2021 a new program to standardize fT4 measurements. CDC ensures that the program is linked to the IFCC C-STFT by being a successful member of the reference laboratory network.

The TSH harmonization in Japan is linked to the IFCC C-STFT harmonization panel.

B2: Reference material providers such as NIBSC (UK) and NIST (USA) collaborate with the IFCC C-STFT reference system for reference material characterization.

B3: Accuracy-based EQA providers in the Netherlands and the U.S. use the IFCC C-STFT reference laboratory network for fT4 for target value assignments.

C1: The reference intervals established in Japan as part of TSH harmonization are as of 2021 officially been used.

While C-STFT successfully reached out to EUTHyroid, CDC (USA) and to groups in Croatia and France, little progress was achieved in 2021 due to the lack of available standardized fT4 assays and harmonized TSH routine assays in these countries or regions.

Furthermore, new studies and data collections are hampered by the COVID-19 pandemic, which prevents collection of specimens from volunteers.

D1: The website C-STFT is currently under revision, it is the intention to revise and make it more accessible for a broader type of readers. Progress was delayed due to COVID-19 changes in priorities. Revisions is planned to be finalized in 2022.

D2: Paper about the work of the committee was published for publication.

D3: We conducted a workshop at the annual AACC meeting, September 19-23 2022.

D4: Katleen Van Uytvanghe represents the C-STFT in an ATA working group that prepares a manuscript that will give an update of current practices on thyroid hormone measurements

D6: Using the information available from C-STFT, committee members promote standardization to the C-STFT reference system with the local/regional stakeholders.

List planned activities in 2022 for Term of Reference 1

A: Formalize the operational rules for the fT4 network of reference laboratories. This includes network protocols and ISO compliant SOPs. The individual laboratories will publish their candidate reference measurement procedures, and the network will publish the method comparison study.

Complete specimen collection and characterization of the harmonization panel for the new TSH harmonization panel, with a link to the IU units established with the NIBSC reference materials. Continue sample collection of TSH specimens.

B: Ensure, national/regional standardization efforts are linked to the IFCC C-STFT reference system through participation in the fT4 reference laboratory network, calibration of TSH assays using the C-STFT harmonization panel.

C: Coordinate with principal investigators to ensure reference interval studies and epidemiological studies are conducted with standardized and harmonized assays where available.

Develop statistical and operational approaches/protocols to align ongoing reference interval activities to the IFCC reference system as interim until assays are standardized/harmonized.

Provide technical assistance to national efforts developing reference intervals or conducting studies that may be used for developing reference intervals.

D2: Share C-STFT work and findings through presentations at scientific meetings such as the Worldlab conference in Seoul and the AACC meeting in Chicago. Give one educational IFCC webinar on work and progress achieved by C-STFT in second part of 2022

D3: Conduct 2 C-STFT meetings for members and stakeholders.

D4: Update website to better communicate changes associated with FT4 standardizing and TSH harmonization.

D5: Represent C-STFT work through participation with stakeholders such as the ATA working group.

C-STFT plans to have again two meetings.

Plans are to have a in person/hybrid meetings in conjunction with WorldLab in Seoul 2022 (26 – 30 June) and the IFCC General Conference in Brussels (27 – 31 October 2022)

A proposal to organize a scientific session on thyroid hormones at next year's AACC 2021 (Sep 19-23) will be made.

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

Program Manager: BD

IgG anti beta-2 Glycoprotein 1 material

The report for WHO regarding the candidate reference preparation for anti beta2 glycoprotein 1 has been prepared by Dr. Evi Monogioudi (JRC) will be sent to Lucy Studholme (NIBSC) for checking. The next step in the process if for it to be submitted to the WHO on the 11th of February 2022 or the subsequent meeting in June 2022 (hopefully the February meeting).

IgG anti glomerular basement membrane material

Dr Evi Monogioudi (JRC) has prepared a report on the commutability of the candidate base materials and one of these has been selected. We will discuss the use of this material with Prof Charles Pusey on Jan 11th and after that a decision will be made about progressing with this material.

IgG anti MPO (ERMDA 476/IFCC) and IgG anti PR3 (ERMDA 483/IFCC)

Much as we have expected, there has been limited uptake of these materials. This remains a complicated issue. One company, Thermo Fisher has a large part of the market and they are completely against using this material; they use their own units (that are essentially arbitrary) and their technology uses a single standard curve for all the IgG antibody assays so are resistant to any changes. There is still considerable stock of these materials in the JRC.

Sales 476: We still have 2489 vials

Sales 483: We still have 3165 vials

There have been no meetings to attend or present at.

PG commented that all members of this committee and the Chairman reach the end of their terms at the end of 2022. The committee needs to be completely renewed, or maybe create a new committee or WG. BD suggested combining C-HAT with new immune markers together.

MR commented that anti-CCP is just starting and publication is being prepared about new standardisation material

8.2.27 C-BONE METABOLISM (C-BM)- Appendix 1

Program Manager: KM

PG commented this committee was formed three years ago combining different WGs; all members approach the end of their 1st term. All members and chair will continue into their second term until the end of 2024.

RJ informed the committee that PTH is a project plan within CCQM and the protein analysis WG is going to have a purity study on PTH 184 and started discussions before pandemic but were then

put on hold; now things are starting again; already in discussion with the CDC and NSC will provide material. This will happen over the next couple of years.

8.3 WORKING GROUPS

8.3.35 WG – STAND. OF HEMOGLOBIN A₂ (WG-SHbA₂) - Appendix 1

Program Manager: KM

PG commented he has discussed the situation with Andrea Mosca who informed him that the method will be accepted to be JTTLM listed; this point is very important. This work should be finalised in the near future.

8.3.36 WG - STAND. OF CARBOHYDRATE-DEF. TRANSFERRIN (WG-CDT) - Appendix 1

Program Manager: CC

PG commented there is no information regarding the date of their next meeting; he will contact the chair to ask.

ACTION: PG to write to the Jean Deenmamode of WG-CDT to ask for the date of the next meeting.

8.3.39 WG – STAND. OF ALBUMIN ASSAYS IN URINE (WG-SAU) - Appendix 1

Program Manager: GM

GM commented that this project is in collaboration with NIDDK which is chaired by GM; currently in the process of organising a meeting of reference laboratories developing a reference procedure for urinary albumin to conduct a sample sharing exercise in preparation for a larger “round robin” exercise. This meeting will happen in the next few weeks. Hopefully the “round robin” exercise will finish late Spring or Summer this will give them the information for JCTLM submission probably in May 2023

KM confirmed that they have completed all of the certification processes; the work on shipping conditions has progressed well.

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

Program Manager: BD

PG commented that the commutability study is yet to be done. This should have been closed last year, but due to the pandemic this was not possible. He has asked the EB for an additional year which was agreed; this WG should complete its activities in 2022 and then be closed. Dr Friis Hansen will take over as chair for one year to finalise activities.

8.3.41 WG – GROWTH HORMONE (WG-hGH) - Appendix 1

Program Manager: CC

CC informed the committee that there is a new Chair and is working as expected. The last few months the WG focussed on setting up a new comparison for GH measurements using immunoassays from all major diagnostic companies compared to candidate RMPs. A preliminary comparison performed previously showed overall good agreement between methods using patient derived samples. In that study the calibrators used were from pooled patient samples and had some commutability issues at higher hGH concentration. Within CCQM several laboratories running a LC MS/MS hGH method participate and showed a good agreement in a pilot study between their methods. In Q4 of 2021 a meeting will be planned between IFCC WG and CCQM representatives to discuss options for collaboration and the possibility to participate as a site for running an RMP. Within the new comparison planned by the IFCC WG, we prefer that a selected number of CCQM laboratories participate. These laboratories have some variation in peptide-use for quantification of hGH, which could benefit the overall outcome of the comparison. Depending on the outcome the

WG will decide to use a LC-MS/MS method as RMP or use the trimmed mean method for standardization.

ACTION: CC to seek clarification over the use a LC-MS/MS method as RMP or use the trimmed mean method for standardization of hGH.

8.3.42 WG – STAND. OF INSULIN ASSAYS (WG-SIA) - Appendix 1

Program Manager: CC

The latest report dates back to last October; this is being worked on in the University of Minnesota. They are working with WHO (Gwen Wark is involved) on setting up a reference material for insulin, so they are working on the basis of standardisation. CC commented that she hopes this is not just a single calibration laboratory being used for their studies.

PG stated we should discuss this during our next meeting.

ACTION: PG to ensure this is discussed.

8.3.43 WG – STAND. OF TROPONIN I (WG-TNI) –

Program. Manager: IY

IY spoke to the submitted report:

The objectives of this workgroup have been to:

1. Design RM 8121, which will be a set of four (4) commutable cTnI-containing samples with concentrations: (i) between the Limit of Detection and Female 99th percentile upper reference limit (URL); (ii) +20% of the male cTnI 99th percentile URL; (iii) 5-fold higher than the male 99th percentile URL; and (iv) between 5500 and 6500 ng/L with the Siemen's Atellica TnIH assay. This design was a collaborative design between NIST, the International Federation for Clinical Chemistry and Laboratory Medicine (IFCC) Workgroup for cTnI standardization, and Dr. Robert Payne.
2. Collect blood from MI patients containing high concentrations of cTnI under an Institutional Review Board (IRB) protocol approved by both the University of Maryland Baltimore IRB and the NIST Ethics committee.
3. Collect blood from normal healthy individuals sufficient for blending with the elevated MI patient samples to produce RM 8121, under a protocol approved by both the University of Maryland Baltimore IRB and the NIST Ethics committee.
4. Collect sufficient amounts of samples in Objectives 2 and 3 to produce between 2500 to 3500 vial (0.7 mL each) sets of RM 8121.
5. Work with NIST personnel to oversee the proper blending and production of 2500 to 3500 four-member sets of RM 8121 at the appropriate cTnI concentrations.
6. Work with NIST personnel and stakeholders to assign high sensitivity (hs) cTnI values to each of the four vials comprising RM 8121. Disseminate message about availability of material and values.

Objectives achieved to date:

1. Objective 1 is accomplished: TnI-containing samples with concentrations as stated in objective 1 above have been collected. The ideal matrix was determined to be Lithium heparin plasma after consultation with the IFCC committee and experts in the Laboratory Medicine field.
2. Objective 2, accomplished. Under IRB protocol HP-00080694 at University of Maryland Baltimore (UMB) and also by the NIST Human Protections Research Organization, sample collection was completed from MI patients with elevated cTnI levels are available in quantities sufficient to meet objective one. All samples were screened and shown to be free from infectious Hepatitis A,B,C and HIV.
3. Objective 3, accomplished. Under IRB protocol HP-00090329 at UMB, sample collection was completed from normal volunteers that provides a commutable low cTnI concentration blending

material in quantities sufficient to produce the sets of RM 8121 in objective 1. This protocol was also approved by the NIST Human Protections Research Organization. All samples were screened using FDA cleared methods and shown to be free from infectious Hepatitis A,B,C and HIV.

4. Objective 4, accomplished. Calculations were conducted and triple checked that sufficient amounts of human samples with elevated cTnI from MI patients (Objective 2) and normal healthy individuals (Objective 2) to produce 3150 sets of 4 vials each, each vial containing 0.7 mL of RM 8121. All materials are stored at -70 deg C in freezers monitored 24 hours a day 7 days a week with remote alarms to directly alert study personnel in case of malfunction. A backup plan has been developed in case of freezer failure. All human materials collected for production of RM 8121 remain in Dr. Christenson's monitored -70 deg freezers as of 06-November-2021.

5. Objective 5, has been accomplished in part. According to Dr. Mark Lowenthal, the lead collaborating NIST scientist, NIST has awarded the funding for bottling / blending / testing of the cTnI materials. The contractor's name is Solomon Park Research Labs; NIST has successfully worked with this organization in the past to "great success".

6 Objective 6. Assess the presence of autoantibodies and like interferences that impact cTnI recovery in the human plasma from normal subjects, i.e. samples that will be used for blending RM 8121.

Progress toward Objective 6. On 10-June-2021, we shipped 1-mL aliquots (separated at the time of collection) of each collection from the normal healthy human subjects procured in Objective 3 to HyTest LTD, to Turku Finland to test for cTnI antibodies in these samples. All samples were packed in dry ice and shipped in accordance with HyTest's instructions. Receipt of these samples frozen and in good shape was acknowledged by Antti Kulta at HyTest. However, as of over 120 days later (date of this report; 06-NOV-2021) we have not yet received results back from HyTest despite numerous requests for an update on the status of the measurements.

Both Dr. Mark Lowenthal and I have separately and together, contacted our HyTest representative, Dr. Alexey Katruka numerous times and asked for the status of the project. Because of this delay, we have designed an experiment to assess autoantibodies and other interferences that impact recovery of cTnI, in each normal sample to be used for blending. This experiment will examine two cTnI positive of pools having values in the range of the male and female 99th percentile cut-offs. The positive cTnI solutions would be mixed 1:1 with each of normal samples intended for blending of the NIST RM 8121. We will measure the mixed samples and the pools, and assess the cTnI recovery. If the recovery is not lower than calculated (including uncertainty), then the sample will be deemed to be appropriate for use in producing RM 8121. All collections from normal healthy individuals will be tested in this way. This method was reviewed and agreed upon by NIST.

After determining which normal samples collected in Objective 3 are appropriate for use in producing RM 8121, we will be able to work with Solomon Scientific to ship them the samples for blending the samples that will comprise RM 8121, and for filling and labelling vials with 0.7mL each level. Working with NIST personnel and stakeholders, values for high sensitivity (hs) cTnI values will be assigned to each of the four vials comprising RM 8121. Then a message will be widely and transparently disseminated message announcing availability of RM 8121.

Summary: We are ready to make this RM available and plan to complete production of the material shortly after the holidays, in early 2022. We will keep the IFCC Scientific Division apprised of the progress.

IY summarised the WG is making good progress; they are working with Solomon Parks in the US to collect samples in terms of preparing a sample with NIST. One objective is where they have become stuck is identifying autoantibodies and similar interferences in the samples that might impact on TnI recovery. In June 2021 sent samples to High Test in Finland to test for Abs; there was acknowledgement of sample receipt, but no results have been received despite several attempts to contact them. They are developing an alternative approach. They are in a position to make a reference material available with plan to complete production early 2022.

CC commented that there was a Zoom meeting between Cardio Met and the WG. It was agreed that Claudio will become a consultant on the WG.

8.3.49 WG – CSF Proteins (WG-CSF)

Program Manager: MP

No update received from this WG

ACTION: PB will ask for an Annual Report

8.3.51 WG- COMMUTABILITY IN METROLOGICAL TRACEABILITY (WG-CMT) **Appendix 1**

Program Manager: *To be determined*

GM: Group is active with two meetings planned in coming weeks, currently working on criteria to be used for making a feasibility assessment split work into two papers (certified reference materials and EQA materials), there are draft manuscripts, not ready to submit yet but within coming months draft copies will be submitted to SD, NIST and CDC.

8.3.52 WG – IMMUNOSUPPRESSIVE DRUGS (WG-ID) - **Appendix 1**

Program Manager: MP

There has been no report from this committee; it was planned to meet the Chair during the now postponed Munich meeting where he was to be a speaker. A meeting will now be organised in April at the postponed Munich meeting.

ACTION: PG to organise a meeting with the Chair of the WG-ID.

8.3.54 WG – APOLIPOPROTEINS BY MASS SPECTROMETRY (WG APO-MS) - **Appendix 1**

Program. Manager: KM

CC (December) raised the publication strategy from IFFCC WG on lipoproteins (LPs) by MS; tried to develop a RMP for 7 different lipoproteins including Lp(a). This is a massive endeavour to develop a single RMP for several LPs, and for developing the primary and secondary reference materials. As the approach is so large there is a publication strategy in which they wish to communicate their way towards a JCTLM RMP, the SD will be sent different publications. First reactions on measurement procedure paper were obviously not well understood, so things will be broken down into several papers and will be sent to SD members. Because of complexity the WG will take a stepwise approach first IFCC then JCTLM. CC is concerned that they are being judged on the end result which is not there yet. There is a priority in which LPs are looked at first. The step by step procedure is shown in PowerPoint file below. IY raised the historical problems caused by CDT endorsed by IFCC but failed to achieve JCTLM listing; possibly one of the issues of this sequencing is it raises the possibility unless the IFCC endorsing procedure is done by JCTLM procedure.



Microsoft PowerPoint
97-2003 Presentation

CC (January) Develop a high order RMP for: Apo(a), Apo A-1, Apo B, Apo C-I, Apo C-II, Apo C-III and Apo E. Decided on an immune assay independent candidate RMP based on MS with bottom up proteomics. Take a two pronged approach, one on the procedure and the other on materials; as seven analytes are involved the publication strategy must not wait for everything to be published, therefore publications will have a phased rollout. Method development was a lot of work taking many years; decided to write about method development and validation independent of the development of primary and secondary reference materials. Two papers are now ready for submission. Mainly focussed on Lp(a) followed by Apo A-1 then Apo B. Working in three calibration labs so care is taken over comparison. For IFCC endorsement the Traceability Chain must be in place, and need to have an established primary reference materiel.

PG suggested we support the procedure proposed by CC.

PG commented that it is important to recognise the global strategy. CC highlighted that there is a lot of work for collaborating labs; the challenge will be for collaborating labs to identify resources, but work needs to be done to ensure continued involvement of the laboratory network. Hopefully all labs will remain within the network; otherwise new laboratories need to be identified; but appears that labs remain committed. IY asked if there has been successful collaboration with manufacturers. CC stated that currently most work has been with the larger manufacturers, many of them are corresponding members of the WG. LD commented they have done preliminary commutable experiments; recombinant materials are not suitable so need to go with human donations. When they have the final secondary materials they will do another commutability study with more manufacturers. There is very good correlation between MS and immunoassay methods.

ACTION: PB to forward the two Lipoprotein papers for comment.

8.3.55 WG - PANCREATIC ENZYMES (WG-PE) - Appendix 1

Program Manager: CC

CC reported the WG is making good progress in developing and validating a PRM for Pancreatic Amylase the successor of total amylase with a specific pre-analytical step, they hope to publish before the end of 2022. They also performed an international survey but data is not available yet; it looks into the clinical use of these markers; there is great variability in how these tests are used.

8.3.56 WG FECAL IMMUNOCHEMICAL TESTING (WG-FIT) - Appendix 1

Program Manager: PG

PG reported the group is very active, but there is no information on recent meetings. There will probably be a meeting in Munich.

LD commented there has been an on-line meeting of the whole WG; discussed the results of a correlation study of commercial methods to see if they measure the same and there are no interferences. The results have been presented to the manufacturers and they agree we can publish the results; there is a significant bias which may be improved by calibration; but this bias does mean a common cut-off cannot be used at present.

Accomplishments for Term of Reference 1

The analytical work and data analysis has all been completed for the harmonisation/ commutability study. The work was carried out by a small sub-group of the IFCC FIT WG. A report has been compiled and was sent to the four manufacturers of the FIT systems included in the study in October 2021. Individual meetings are being held with each company if requested. A summary of the results will be presented to the IFCC FIT-WG members at the next meeting in November 2021 in Munich.

List planned activities in 2021 for Term of Reference 1

The next stages of this study will be discussed at the IFCC FIT WG in November

Accomplishments for Term of Reference 2

No progress made in 2021

List planned activities in 2021 for this Term of Reference

The FIT-WG will aim to engage with EQA companies to obtain guidance on requirements in terms of EQA to help inform the recommendations formed from the group

8.3.57 WG CELL FREE DNA and related circulating biomarkers (WG-cfDNA) - Appendix 1

Prog. Manager: MP

PG stated he is concerned about the poor activity of this WG, MP has informed PG that he has never gets feedback from the chair. Overall the WG is not active and as such should it be closed? Prof. Dr. Ron H.N. van Schaik (Chair) provided details of member's activity:

1. Members of the working group (RvS, RD, MdR) have convened at the IATDMCT Rome meeting on Sept 20, 2021 to discuss developments on cfDNA field and potential activities of the WG.
2. RvS joined the European Society of Liquid Biopsy in order to maintain contact with developments in the field and inform the IFCC WG.
3. RvS is member of the Dutch COIN consortium that aims at implementation of cfDNA analysis in the Netherlands (€ 3,000,000 project), with contact with European Groups aiming at this in the European setting, transferring the knowledge to the IFCC WG.
4. EL is organizer of the yearly Circulating Tumor Cell symposium that took place this year in September.
5. RvS is organizing the 4th Dutch cfDNA Symposium (January 28, 2022)
6. Individual members have published key papers on cfDNA
7. During EuroMedlab, members that are present will meet in Munich in a live meeting to discuss activities on cfDNA.
8. A full working group meeting is scheduled to take place virtually on Dec 17, 2021 (14:00-15:00) to set aims and strategy for 2022. Regarding your message, I have added "Prolonged existence of the WG?" for discussion on the agenda.

So in total, the WG will have convened 3x in 2020.

PG commented there are a number of personal activities, but nothing specific relating to IFCC activities. This was communicated to Prof. van Schaik, during a teleconference a number of discussion points were raised:

Do we feel there is still a need for this WG in IFCC? ANSWER: Yes

Do we want to continue with the WG? ANSWER: Yes

Is the current membership still OK? Should we expand? ANSWER: Yes

Do we need another chair? ANSWER: No

What could be the next actions/activities to perform for 2022? A number of activities were identified

But PG asked is this a group for SD or would this be better placed in ED? This should be discussed further to include the input of MP.

8.3.58 WG STANDARDIZATION OF PROCALCITONIN ASSAYS (WG-PCT)- Appendix 1

Program Manager: KM

KM summarised that the WG has made good progress, it has developed a stable isotope dilution MS method, this has been published. Now they are working on the sensitivity of the method as now it is only 0.25mg/mL and they want it to be more sensitive. Plan now is to finalise the sensitivity experiments and submit to JCTLM. The next part is to investigate why there is so much variability an working with EQA providers they have published a paper in CCLM in 2021; showed different EQA providers have difficulty in providing commutable material thus resulting in variation. In 2022 they will perform a commutability experiment, but COVID is making this difficult.

PG agreed this is an active group and the problems faced are challenging. The publications mentioned have not been seen by SD. We should remind the WG that manuscripts should be shown to SD before submission for publication. It is important to ensure IFCC is correctly referenced.

MR fully supported the commutability experiment, stating this is very important for manufacturers.

ACTION: KM to remind the chair of WG-PCT to send proposed publications to SD.

8.3 60 WG CONTINUOUS GLUCOSE MONITORING (WG-CGM)- Appendix 1

Program Manager: KM

KM informed the committee that the meeting of this WG will be on 17th January; we will get more information next week. PG reported that the group is active and are preparing a clinical study. KM stated the fundamental issue is what will be the reference method to anchor CGM. The reference method used for calibration is no longer available on the market,

ACTION: KM to forward information from the January meeting of the WG-CGM

8.3.61 WG DEVELOPMENT OF A REFERENCE MEASUREMENT SYSTEM FOR SUSTAINABLE PT/INR STANDARDIZATION (WG PT/INR) - Appendix 1

Program Manager: to be determined (CC Chair)

CC summarised the position; the WG is active with a lot of interest from IVD companies and EQA organisers, There are medical experts involved. The group is working on the WHO method; and with reference to harmonisation there are four calibration labs involved (Roche plus three others). Good progress in lowering the variability, the group is working to refine the method details, as with this method standardising details are important. Starting looking into true standardisation rather than the current harmonisation. Discussing what type of primary reference material will be best, and looking at secondary reference materials investigation different types of thromboplastins used across the globe as this has to be a global solution.

The report was also sent to ISTH subcommittee on coagulation.

8.8 PROJECT PROPOSALS

Project Proposal on “**Standardisation of brain natriuretic peptide (BNP) measurements**” (already circulated on December 3rd) - **Appendix 1**

KM commented this is not the final composition of the proposed WG; he believes this is an important WG. CC stated there is certainly a clinical need for standardisation; but also need to take into account stability and recommends that this should not only be metrology but need clinical laboratory personnel. GOC, EQALM and industry must be included.

PG suggested the KM should discuss comments given with Milena Quaglia. And KM will be the link to ensure that the group is composed of the right members. This proposal should be completed to include all stakeholders before approaching the EB for approval. PG would prefer to wait to get full proposal including returned comments and stakeholder representation before progressing.

ACTION: KM to discuss composition of WG with Milena Quaglia and resubmit to include all stakeholders.

8.40 OTHER BUSINESS

KM raised the issue from last meeting on HbA1c; GJ stated that he planned to meet with KM during the Munich meeting, but as this did not happen the opportunity was lost. GJ stated that he was unsure for the reason behind re-looking at HbA1c standardisation; this has been finalised for some years, and if this standardisation was to be re-investigated would lead to significant uncertainty in the clinical sectors. PG agreed that this is a real concern; saying that maybe people in the Metrological societies believe the RMP is not robust and there may be other approaches; but also warned we have worldwide standardisation with guidelines and diagnostic criteria are anchored by this RMP. GJ stated that there is a stable global network of reference laboratories and results over many years have been very reproducible. He is concerned we would create

problems and undermine the clinical situation if we mess with the system and potentially change values even slightly. There is a lot of confidence in what is currently done in what is a stable network.

PG stated we have to approach this carefully.

RJ stated CCQM have a proposed study on Total Hb, which was a pilot study and discussions are ongoing with JCTLM to meet their requirements, as well as IFCC. CCQM studies are usually in the “back line” if you look at the Protein Analysis WG is a young group and first studies are coming, and they presumed if a study was accepted there it had already been accepted by clinicians in the way it was done. He commented they need to be more careful, especially as there are more funding channels. It will be important to bring partners together

PG stated that it is important to involve the clinical societies before deciding on projects. KM stated the proposed HbA1c study was not questioning the standardisation of the assay but a study to assure all participating labs were able to measure HbA1c “correctly”. RJ stated that the CCQM is there to ensure Metrology institutes can prove their measurement claims. So they use surrogate analytes to prove this.

Going forward it is important that RJ is now a member of the committee.