IFCC C-STFT 2022 HYBRID MEETING

Friday, October 28, 2022
IFCC General Conference
Brussels, Belgium

Meeting Minutes

1) **Welcome and Introduction**
In-person participants: **Hubert Vesper** (CDC, USA), **Katleen Van Uytfanghe** (Ref4U, Ref Lab Network, UGent, Belgium), **Stefaan Marivoet** (Tosoh, Belgium), **Stephan Fellner** (DiaSys Diagnostic System), **Stine Andersen** (Aalborg University Hospital, Denmark)
Virtual participants: **Uliana Danilenko** (CDC Ref Lab Network, USA), **Teun van Herwaarden** (Nijmegen Ref Lab Network, The Netherlands), **Fidelia Pokuah** (CDC Ref Lab Network, USA), **Ashley Riberia** (CDC Ref Lab Network, USA), **Veronique Raverot** (Hospices Civils de Lyon, France), **Akira Hishinuma** (Japan Society of Clinical Chemistry), **Violeta Raneva** (ReCCs), **Gordon Avery** (Abbott, UK), **Paul Williams** (Australia), **Theodora Davy** (Diasorin), **Vincent Chen** (Snibe, China), **Carol Dauscher** (SIEMENS), **Nino Bekaia** (Laboratory Medince Aossciation of Georgia - GLMA), **Barnali Das** (Relianceada, India), **Ron Archer** (Beckman Coulter), **Jian Xie** (Mindray), **David Kiaei** (Siemens Diagnostics), **Tao Yang** (Maccura, China); Zang Min Jin; Snibe, SDS
Michael Rottmann (Roche Diagnostics, Germany), Mindray

2) **Approval of Meeting Minutes from Seoul Meeting [Dr. Van Uytfanghe]**

Approved

3) **Review of Terms of Reference [Dr. Van Uytfanghe]**
Dr. Van Uytfanghe reviewed the term of reference and shared that the main focus of C STFT is to implement and maintain the reference system developed by IFCC Committee and and to support the stakeholders with conducting standardization and harmonization activities.

C-STFT developed a reference measurement system (RMS) for <u>free T4</u> that conforms with ISO 17511. So there exists a primary reference material which is used to calibrate reference measurement procedures (RMP), which in turn can be used by the manufacturers for the standardization and verification of their master, working calibrators and in-house methods and further down to the methods which are used in clinical practice A network of laboratories implementing the free T4 RMP is established and maintained. The task of the C-STFT here is to maintain the network of reference laboratories. As such, at all times interested parties have access to the RMS.

<u>For TSH</u>, the RMS is also ISO 17511 compliant. However, it relies on a panel of human serum panels which forms the basis of harmonization. The latter are value assigned as a joined effort between as much as possible manufacturers, and in overlap with previous panels. Sustainability of the RMS needs a continues flow over time of value assigning targets to new follow-up panels – the task of the C-STFT is to coordinate this continuous effort.

4) **Updates on Project: Develop and establish follow-up panel for TSH [Dr. Van Uytfanghe]**

Over the past year, we have been preparing for the 3rd TSH Harmonization panel. Objective of the panel is to ensure continuity of established calibration set-point using a third harmonization panel and linking third panel to second panel through overlapping measurements.

- Note: The first TSH panel was established in 2015 – the feasibility of the use of such a panel as basis for harmonization was published in 2017 in Clinical Chemistry. At same time a 2nd follow-up panel was created with 95 samples, which were assigned target values in overlap with the harmonization panel. The 2nd panel was meant to be used by all manufacturers to actually verify or work further on the harmonization of their assays.
- At this point of time, we will target the 3rd panel. We will use primarily the same protocol and requirements as we have used in the previous study and use samples covering the entire measurement range and samples close to the limits of quantitation.
- Protocol has two phases:
  - 1st phase (2023 IFCC TSH Study Phase 1, 2023 ITS Phase 1): allow to verify the status of harmonization against the target panels; recalibrate the assays to the target panels, characterization of the candidate 4th WHO international standard for human TSH (81/615). Manufacturers were contacted in September 2022 for participation: 16 IVD manufacturers interested, samples were be shipped in November/december 2022.
  - 2nd phase: Value assignment of the 3rd TSH harmonization panel, which will be provided in a second shipment.
- Sample details for 1st Phase:
  - 86-91 sample set aliquots randomized for concentration and origin divided among participants, along with detailed instructions and reporting template: 0.50 mL aliquots with concentration between 0.002 – 168 mIU/L; along with (1) ampule each of the 3rd (81/565) and 4th(81/615) Candidate WHO international Standard for Human TSH
  - Samples will be sent by CDC and participants can invoice IFCC for the associated shipping cost. Invoices will have to be paid by the manufactures and can be reimbursed by the IFCC. *Redactional note: Dr. Van Uytfanghe will contact all participants in January 2023 to arrange the reimbursement.*
- Status of TSH sample collection for 2nd phase: 5 active collection sites, however due to COVID and other administrative red tapes, some sites are pending collection
  - Samples overview: at least 20mL of serum per individual donors. The aim is to collect more samples with low TSH concentrations, currently we have 10% more samples in the low concentration range compared to the harmonization panel in 2017. However there are less samples with high TSH concentration range (values >50 up to 100 mIU/L (Note, this is challenging patient category because normally these are put on medication asap))
  - Aim for total of 132 samples. The measurement protocol will be designed in such a way that samples will be divided over 16 participants, totally randomized, so that for each sample a total of 5 results per sample is available. As such, we are able to safe enough material for future use.
- Comment was raised that when information is sent to the various participating sites, to include the STFT POC in the communications as well, for awareness and also to accelerate and bridge appropriate personnel.

5) **Updates on Project: Establishment of a reference laboratory network for FT4 [Dr. Van Uytfanghe]**
Aim is to sustain the network of FT4 reference laboratories. The different members of the network provide different services to all interested parties. So as an IVD manufacturer, provider of QC materials, … you can actually work with the different laboratories within the network.
   - 4 Network members: CDC Clinical reference laboratory - USA; Radboud University Medical Center of Nijmegen -The Netherlands; Reference Material Institute of Clinical Chemistry Standards - Japan; Ref4U, Ghent University - Belgium
   - Requests to join network from Autobio-China and Government of Western Australia, and others
     Redactional note: The C-STFT will launch a joint project in spring 2023 to perform a preliminary assessment of the candidate members.
   - Activities:
     - Performed a second network method comparison with samples spanning a broad range of FT4 concentrations. This was primarily done to actually demonstrate that it is possible to have an agreement amongst results in very different laboratories applying methods which are based on the conventional method. Apart from the dialysis, labs differ a lot in the details and still the results are in very good agreement, even though each lab uses independent calibrations – the latter demonstrates strength in the network.
     - Developing network publications and refining RMP SOP based on feedback from network labs, formalizing network rules and establishing method protocols for regular method comparisons
       - Over last few months few requests to join network: will set up some initial experiments for those interested in implementing the candidate reference measurement procedures for FT4 and welcomes additional laboratories to join the network.
     - Sustainability of RMP: evaluate impact of different supplies on measurement accuracy
       - Different membranes (molecular weight cutoffs); ED cells and related hardware; and primary calibrators (issues with availability with primary calibrator)
       - Initial data suggests different membranes and ED cells designs provide equivalent results
       - Manuscripts underway

6) **Updates on Project: Educational activities [C-STFT Committee]**
   - Create awareness about the importance of standardized/harmonized FT4 and TSH assays;
   - Prepare stakeholders about potential changes in values as a result of recalibration; and
   - Inform stakeholders about the IFCC C-STFT and national/regional organizations conducting standardization/harmonization
   - Activities and event:
     - American Association of Clinical Chemistry - sessions and presentations to inform about the IFCC activities on harmonization of TSH and FT4 standardization
     - PATH – partnership with about 50 organizations - inform about IFCC activities and received support of local activities of the American Thyroid Association:
       - ATA writing group – working on manuscript on basic overview of thyroid hormone measurements, which measurements to do, which quality specifications to apply and inform on harmonization efforts in progress. May led to practice recommendations in the future as a second phase task of the working group.

            - Presented at the 2022 ATA Annual meeting – positive feedback on the work of the committee and CDC; clinicians expressed that implementation of FT4 standardization (values may change for some assays) will not be a real big problem in the calibration change and reference interval changes… so moving to standardize values will be welcomed. Also suggested to look into thyroid antibodies and variabilities that exists.
        - Additional educational activities/communications: CDC CSP newsletter and events, C-STFT website, scientific presentations at EuroMedLab, WorldLab, The Annual Meeting of the European Thyroid Association, ….

7) **Updates on C-STFT Member Activities [C-STFT Committee]**
    - AIM: Global harmonization and standardization for thyroid hormones. However, activities must be done on the regional/local levels to achieve these goals.
        - CDC:
            - Established a HoSt program (FT4 Standardization program) with phase 1 samples- verify performance of assays and working on phase 2 samples for formal certification program
            - Developed Highly accurate and precise routine ED-LC-MS/MS method
            - Measurement of U.S. National Nutrition and Health Examination Survey (NHANES) survey samples using developed routine ED-LC-MS/MS method to develop reference intervals
            - Conducted FT4 Interlaboratory Comparison Study in 2022 results in development and manuscripts are in progress
            - Participants of the CDC FT4 Interlaboratory Comparison Study received preliminary results for their assay (all other participants were blinded). The study results will be published
            - Technical assistance to assay manufacturers is ongoing
            - Collaboration with major EQA/PT provider to assign FT4 values for materials used in the accuracy-based survey
        - Japan:
            - ReCCS is establishing the IFCC FT4 RMP in its lab
            - Dr. Hishinuma, president of the Japan Thyroid Association, organized a meeting including 10 in-vitro companies, ReCCs as well as scientific experts on how to establish TSH reference intervals in elderly, young, and pregnant people in Japan and how to standardize FT4 tests.
            - TSH RI for pregnancy, one infertility clinic will evaluate existing data
            - FT4 standardization, ReCCs and 10 companies (members of JACRI: Japan Association of Clinical Reagents Industries) were asked to make serum panels for calibration. JACRI is now working on plans to develop such panels.
        - UGent
            - Continues to provide reference measurements to manufacturers and EQA providers, services are tailored to the needs of the interested parties
        - Radbound University Medical center of Nijmegen
            - Apply their reference measurements procedure and ED based routine procedure to different patient groups with challenging characteristics, i.e. pregnant women

8) IFCC meeting options

   The next C-STFT will be held in conjunction with EuroMedLab: May 22nd 2023, 14u – 18u.
   Details will follow.

   The need for a lively in person meeting was expressed, we would encourage all of our interested parties to join us around the table.

Meeting Adjourn