IFCC Committee for Standardization of Thyroid Function Tests (C-STFT)
Meeting at AACC 2016, Philadelphia, PA, USA, Monday August 1st (12 – 13:30 pm)

PARTICIPANTS

The meeting attendance list, as well as the list with excused people, is attached (Appendix A). The initials used in the minutes are contained in this list.
To avoid that all items dealt with in the meeting have to be repeated, the minutes are best read together with the accompanying slides (see Appendix B).

OPENING OF THE MEETING

The chair (LT) welcomed the meeting attendees. She started immediately with her slide presentation. The slides summarize the data discussed in the reports "Recalibration report C-STFT Phase IV - February 2016" and "C-STFT FT4 and TSH Reference Interval Studies - May 2016".

Editorial note:
As there was little or no discussion during the presentation of the results, the minutes will restrict to the last couple of slides and extensive discussion on the way forward.

(1) Way forward – Question 1: Can we agree on preparing the implementation of the harmonized TSH assays?

Can each IVD-company representative on the C-STFT obtain a formal agreement of his/her management?
What timelines are feasible?

- (YC) From a regulatory point of view, if the change for an assay after harmonization is NOT major, internal documentation will be sufficient to obtain a new FDA clearance. However the FDA will evaluate this for each manufacturer individually. As for most assays the changes are within 10% (MR) and within the limits for acceptable changes commonly set by the manufacturers (PS), no major shifts after harmonization are to be expected. This was confirmed by the FDA (YC).
  LT repeated that it will be crucial to mention, when entering in contact with the FDA, that the assay participated in the C-STFT method comparison study. This will allow the FDA to appoint the same team of referees for the different manufacturers. YC stated that she can be contacted directly, of course the FDA, in general, can also be contacted.
  Later on in the discussion it was agreed that the manuscript, describing the method comparison and reference interval (RI) study for TSH, can be part of the internal documentation of each IVD-manufacturer.
- MR questioned the benefit of the harmonization effort for TSH, when the changes are within 10%. GB replied that harmonization is needed, as currently, international guidelines use specific numbers for the TSH reference ranges/decision points. Although the differences are not big, some patients may fall aside these decision points either side, depending on the assay used. MR further discussed that the debate on subclinical lower and upper limits, as well as on the upper limit of the normal TSH range in general will continue. According to GB, our project will help in better/definitively defining these decision points.
- MP questioned whether the RI will be the same for each manufacturer. LT reminded that this RI study was only intended as a basis for further in depth studies. Therefore, the samples had not been selected with the highest carefulness. Indeed, they were not screened for all possible thyroid antibodies (only for anti-TPO). GB confirmed that further studies on the RI will be needed, e.g. to account for ethnicity,

age,…
According to MR, based on the results shared up to now, it is too early to answer question 1. The data should first be made publicly available and serve as a basis for discussion with end-users. LT replied that we are preparing 2 manuscripts, one on the phase IV method comparison and recalibration exercise (both TSH and FT4), one on the RI (both TSH and FT4).
Editorial note: in follow up of further discussions, the manuscripts will be rewritten. In essence, we will split them in 2 parts, one manuscript for TSH and another for FT4. The former will be given the highest priority. By dealing separately for TSH and FT4, it will be possible to combine the report on the method comparison study, the recalibration exercise and the RI study.

- MR also stated that more awareness on the C-STFT should be created, this will help to have a more profound discussion with the stakeholders. It was generally agreed that the two publications will facilitate this.
- LT confirmed that each manufacturer will receive the draft manuscript for review, prior to submission. She will carefully read the comments/requested amendments and try to account for all of them. However, as there may be comments coming in from 14 manufacturers (2 just recently joined and are measuring the Phase IV samples at this very moment), she cannot guarantee that each single comment will be accepted. She will finally decide in good conscience. LT also reminded to the fact that the identity of all manufacturers' results will be disclosed in the manuscripts. All manufacturers agreed with this as they did already in the past.

(2) Way forward – Question 2: FT4 - Do manufacturers agree that improvement of their assays may be needed before implementation?
What timelines are feasible?

- (LT) Can we agree to postpone the standardization of FT4 assays? The advantage will be that the long promised second reference laboratory (CDC) can catch up (note from LT: since recently Dr. M. Umemoto, director of Reccs in Japan, passed away, the previous collaboration with the Japanese reference lab was temporarily set on hold) and to go for the approval of its reference measurement services by the JCTLM. The availability of 2 reference laboratories will contribute to the sustainability of the FT4 traceability basis. In addition, manufacturers who will need reference measurement services to improve their assay, will in the long term have the option of collaboration with one of the 2 reference labs.
- Several manufacturers also pointed to the fact that more education is needed concerning the changes that are to be expected for FT4. In the following discussion, two major points were highlighted (based on different contacts and experiences):
i) end-users (patients) who get familiar with our work are horrified to find out that the differences between manufactures are currently so big. As they are used to evaluate numbers, without much further information, they can imagine the risk of misinterpretations in the current situation.
ii) professional workers (clinicians, endocrinologists, …) on the other hand state that good communication systems are in place to avoid any misinterpretation once standardization is accomplished.
- The magnitude of the changes to the FT4 values will also have its impact to what documentation is needed to obtain FDA clearance. YC (personal opinion) said that since the FT4 RI has been measured with a reference measurement procedure, it eliminates the requirement for each individual manufacturer to repeat his own RI

study. A verification, based on 20/30 samples, could be sufficient. The C-STFT as a group could make a proposal how to deal with it. MP requested if clear guidance on the requirements for FDA clearance could be given. YC committed that the FDA will have an internal discussion to list the requirements, and get back to LT with it. LT will then share it with the group.
Editorial note: LT can provide discussion materials to the FDA, if needed.

- Concerning the RI, MP also stated that, ideally, we should strive for one RI per region. For this, harmonization/standardization is indeed the ideal basis (LT).
- Concerning the timing, it was also generally discussed that standardization cannot be realized in the very near future, because of the need for extensive discussions to create awareness on the changes that will happen, for collection of extra samples to verify method quality, for an extension of the RI study, for preparing documentation for the FDA clearance, etc. LT also emphasized the need for coordination, so that all manufacturers will implement the standardized assays, at the same point in time, and worldwide.
- LT also noted, that for FT4, the traceability basis is established and will be sustained . Hence, manufacturers will always have the possibility to work with a reference measurement laboratory, if they need to. RJ questioned whether there will be enough capacity in the reference measurement laboratory. LT replied that currently a FT4 follow-up panel is available and under certification. This should last, at least, for the next two years. If, in the meantime a 2nd reference laboratory can be established, then the capacity should be sufficient.

(3) Way forward – Question 3: Further role of the C-STFT?

- Write 2 manuscripts on the Phase IV and RI studies (TSH and FT4, separately) (submit to “Clin Chem”).
- Recruit new IVD companies willing to join C-STFT; guide them through the familiarization-, technical recalibration phase and RI studies.
- Continue the stability study of the panels.
-

- Next C-STFT meeting: parallel to IFCC EuroMedLab, 11-15 June 2017, Athens, Greece (Rationale, limitations in time slots at the AACC restrict thorough discussions).

(4) Way forward – Question 4: Further role of the C-STFT to assess/prove the sustainability of the FT4/TSH “standardization/ harmonization” status?
The Percentiler application is available; are IVD-companies prepared to collaborate and use it?

- LT explained the use of the Percentiler: it is designed to serve as a tool for monitoring the stability of the calibration status of different assays, based on the daily median of outpatient results sent by individual laboratories for each instrument/platform they use; the participating laboratories are grouped in instrument/platform-based peers based. In this way the Percentiler can serve for C-STFT to monitor the recalibration status of the different peers in the post-standardization/harmonization phase. The Percentiler and its use in the pre-standardization/pre-harmonization phase has already been documented in publication form (see references 1-3).

- LT asked whether this explanation is sufficient for the FDA? YC replied that, since the FDA is not yet familiar with the Percentiler, she does not know the answer. LT will send all necessary information to the FDA for internal review.
  LT also stated that, if needed, C-STFT and its IVD-partners would be prepared to organize a second meeting with the FDA.
- LT repeated her request for support from the IVD-manufacturers in order to have all manufacturers/test systems on board of the Percentiler and to substantiate the current peer groups. For obvious reasons, the more laboratories participate per peer, the more reliable and representative the observations in the Percentiler will be. Nevertheless, LT confirmed that currently the peer medians across manufacturers correspond very well with the calibration differences observed between the different manufacturers in previous method comparison studies.

YC concluded that, as FDA representative, she was impressed by the work done by the C-STFT. As the work is done to improve patient outcome, FDA cannot but fully support the project.

Summary of actions-to-take and pending questions to answer:

1. **UGent to prepare the two manuscripts describing the TSH and FT4 phase IV method comparison study, recalibration exercise and RI study (highest priority: TSH).**

2. **Manufacturers to comment on the draft manuscripts.**

3. **Manufacturers to send suggestions for future dissemination of the C-STFT work.**

4. **C-STFT chair to send to the FDA detailed information on the use of the Percentiler.**

5. **FDA to communicate to the C-STFT chair about the requirements needed for clearance of standardized FT4 assays, and to send their recommendations on the use of the Percentiler.**

6. **Manufacturers to help finding more participants for the Percentiler to substantiate the already available peer groups; manufacturers who do not yet have their test systems represented should seek customers willing to participate.**

7. **IFCC secretary (Mrs. P. Bramati) to send the invoices for the scientific secretariat 2016-'17.**

Minutes made by:
Katleen Van Uytfanghe, PhD with help of Linde De Grande, PhD-student
Minutes approved by Prof. Dr. Linda Thienpont, chair of the IFCC C-STFT

Ref4U, Laboratory for Toxicology, Faculty of Pharmaceutical Sciences, UGent
Ottergemsesteenweg 460, B-9000 GENT, Belgium
Tel. +32 9 264 81 21
e-mail: linda.thienpont@ugent.be; katleen.vanuytfanghe@ugent.be;

References

1. De Grande LA, Goossens K, Van Uytfanghe K, Stöckl D, Thienpont LM. The Empower project – a new way of assessing and monitoring test comparability and stability. Clin Chem Lab Med 2015;53:1197-204.
2. Goossens K, Van Uytfanghe K, Twomey PJ, Thienpont LM; Participating Laboratories. Monitoring laboratory data across manufacturers and laboratories – A prerequisite to make “Big Data” work. Clin Chim Acta 2015;445:12-8.
3. De Grande LAC, Goossens K, Van Uytfanghe K, Das B, MacKenzie F, Patru M-M, Thienpont LM; for the IFCC Committee for Standardization of Thyroid Function Tests (C-STFT). Monitoring the stability of the standardization status of FT4 and TSH assays by use of daily outpatient medians and flagging frequencies. Clin Chim Acta 2016 April 27. Doi: 10.1016/j.cca.2016.04.032. [Epub ahead of print].

Appendix A

Name	Affiliation	e-mail address
Aoyagi, Katsumi (KA)	Fujirebio, Inc	km-aoyagi@fujirebio.co.jp
Beastall, Graham (GB)	IFCC EB and representative of the BTA	gbeastall@googlemail.com
Bitcon, Vera (VB)	Siemens	Vera.bitcon@siemens.com
Bosworth, Tracey (TB)	FDA/CDHR/OIR/DCID	tracey.bosworth@fda.hhs.gov
Brown, Nina (NB)	Abbott	Nina.Brown@abbott.com
Budd, Jeffrey (JB)	Beckman Coulter	jrbudd@beckman.com
Chan, Yung (YC)	FDA/CDHR/OIR/DCID	yung.chang@fda.hhs.gov
Chen, Vincent (VC)	Snibe	vincent.chen@snibe.com
Clapshaw, Patric (PC)	Solomon Park	pclapshaw@solomon.org
Das, Barnali (BD)	Member of C-STFT (ACBI; Kokilaben Dhirubhai Ambani Hospital and Medical Research Institute at Mumbai, India)	barnali.das@relianceada.com
Dauscher, Carole (CD)	Siemens	carole.dauscher@siemens.com
De Grande, Linde (LDG)	Ghent University, Belgium	Linde.degrande@ugent.be
Dimagno, Lisa (LD)	Ortho Clinical Diagnostics	lisa.dimagno@orthoclinicaldiagnostics.com
Faix, Jim (JF)	Member of C-STFT (AACC; Montefiore Med Ctr)	jfaix@montefiore.org
Gillery, Philippe (PG)	Member of the IFCC SD	pgillery@chu-reims.fr
Hall, Christina (CH)	Fujirebio	christina.hall@fdab.com
Hishinuma, Akira (AH)	Dokkyo Medical University	a-hishi@dokkyomed.ac.jp
Hollidt, Jörg-Michael (JMH)	in.vent Diagnostics	jm.hollidt@inventdiagnostica.de
Hosimer, Phil (PH)	Ortho Clinical Diagnostics	philip.hosimer@orthoclinicaldiagnostics.com
Ichihara, Kiyoshi (KI)	Yamaguchi University	Ichihara@yamaguchi-u.ac.jp
Janzen, Roland (RJ)	Siemens	roland.janzen@siemens.com
Kutschera, Iris (IK)	Diasorin Inc.	iris.kutschera@diasorin.it
Marivoet, Stefaan (SM)	Tosoh Europe	Stefaan.Marivoet@tosoh.com
Narayanan, Shanti (SN)	Tosoh US	Shanti.Narayanan@tosoh.com
Patru, Maria-Magdalena (MP)	Ortho Clinical Diagnostics	maria.patru@orthoclinicaldiagnostics.com
Raneva, Violeta (VR)	Reccs	v-raneva@reccs.net
Reid, John (JR)	Abbott	John.reid@abbott.com
Rodriguez, Patrih (PR) (representing Adelmann, Annette)	Beckman Coulter	patrihrodriguez@gmail.com
Rottmann, Michael (MR)	Member of C-STFT (Roche Diagnostics)	michael.rottmann@roche.com
Schneider, Randy (RS)	Abbott	randal.Schneider@abbott.com
Sibley, E.C. Paul (PS)	Corresponding member (Siemens Medical Diagnostics)	paul.sibley@siemens.com

Strelkow, Ilja (IS)	in.vent Diagnostica	i.strelkow@inventdiagnostica.de
Suga, Koichi (KS)	Tosoh Bioscience Inc.	Koichi.suga@tosoh.com
Tate, Jill (JT) (representing Williams, Paul)	AACB	jill.tate@health.qld.gov.au
Thienpont, Linda (LT)	Chair IFCC C-STFT	linda.thienpont@ugent.be
Thomas, Chris (CT)	Ortho Clinical Diagnostics	Chris.thomas2@orthoclinicaldiagnostics.com
Tomoko, Ono (OT) (representing Tashiro, Shigeru)	LSI Medience Co.	Ono.tomoko@mv.medience.co.jp
Torres, Marta (MT)	Cemic	mtorres@cemic.edu.ar
Tsukamoto, Hisao (HT)	Tosoh	Hisao-tsukamoto-rn@tosoh-co.jp
Turbeville, Pamela (PT) (representing Ehrenkranz, Joel)	i-calQ	pamela.turbeville@i-calq.com
Van Uytfanghe, Katleen (KVU)	Scientific secretary IFCC C-STFT (Ghent University, Belgium)	Katleen.VanUytfanghe@UGent.be

Excused

Name	**Affiliation**	**e-mail address**
Adelmann, Annette	Beckman Coulter	amandelmann@beckman.com
Ehrenkranz, Joel	i-calQ	Joel.Ehrenkranz@imail.org
Takashi, Kagawa	Sysmex	Kagawa.Takashi@sysmex.co.jp
Yamasaki, Masatoshi	Sysmex	Yamasaki.Masatoshi@sysmex.co.jp
Miller,Greg	Virginia Commonwealth University	greg.miller@vcuhealth.org
Petter Berg, Jens	Oslo University Hospital	j.p.berg@medisin.uio.no
Tashiro, Shigeru	LSI Medience Co.	tashiro.shigeru@mh.medience.co.jp
Tsuura, Masashi	Tosoh	masashi-tsuura-yv@tosoh.co.jp
Van den Bruel, Annick	AZ Sint-Jan Brugge	Annick.VandenBruel@azsintjan.be
Williams, Paul	AACB	paul.williams@sydney.edu.au
Yu, Xiang	Maccura	yuxiang@maccura.com
Long, Tengxiang	Maccura	china-dragon@maccura.com

Appendix B

Slides from the annual meeting in conjunction with the AACC 2016 Conference

IFCC Committee for Standardization of Thyroid Function Tests (C-STFT)

Annual meeting in conjunction with the AACC 2016 Conference

AACC

68TH AACC ANNUAL SCIENTIFIC MEETING & CLINICAL LAB EXPO
July 31 – August 4, 2016
Philadelphia, PA • USA

Chair
Linda Thienpont
Linda.thienpont@ugent.be

Scientific Secretary
Katleen Van Uytfanghe
Katleen.vanuytfanghe@ugent.be

Agenda

Discussion items

- Phase IV method comparison studies for TSH & FT4
- Reference interval studies
- Preparation of implementation – Awareness/Support
- Way forward

Agenda

Discussion items

- Phase IV method comparison studies for TSH & FT4
- Reference interval studies
- Preparation of implementation – Awareness/Support
- Way forward

Phase IV method comparison – Design

RECALL – Target setting

TSH

APTM-11, i.e., calculated from 11 assays by a robust factor analysis method (1 assay excluded)

Alternative: APTM-4, i.e., from 4 assays after pooling of the data for the harmonization and follow-up panel (measured in parallel)

Advantage of using the APTM-4

Targets estimated from 2x the sample-size (n = 196 vs 101) with better distribution of concentrations

Follow-up panel needs no value transfer from the harmonization one ($U_{follow\text{-}up\ panel} = U_{harmonization\ panel}$)

FT4

ED-ID/MS measurements (min. triplicates in independent runs)

Phase IV method comparison – Design

TSH harmonization

APTM-4 or APTM-11?

Impact on the recalibration outcome is extremely small

The means for the panel samples after recalibration of the IAs against the APTM-4 and APTM-11 targets compare well (R^2 = 0.998), with a difference of 1.6%, only

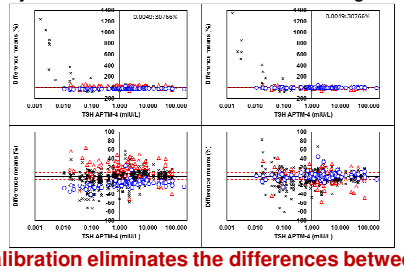
→ APTM-4 preferable

NOTE: Only results based on APTM-4 recalibration will be discussed

Phase IV – TSH harmonization

Recalibration against the APTM-4 targets

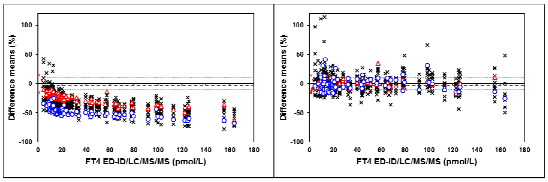
NOTE: only results within the IAs' measurement range are shown



→ Recalibration eliminates the differences between IAs; % differences nicely centered around zero
→ Impact small for most assays

Phase IV – FT4 standardization

Recalibration against the ED-ID/MS targets

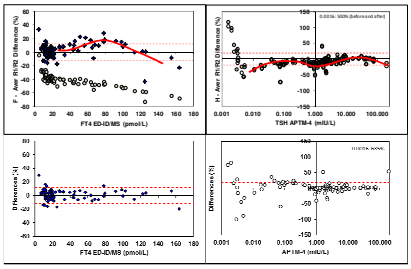


→ Recalibration eliminates the IAs' biases to ED-ID/MS; % differences randomly distributed around zero
→ Impact huge

Standardization/Harmonization

Remark

For some IAs the recalibration is suboptimal (suboptimal recalibration algorithm used?)



Phase IV standardization/harmonization

Recommendations in report

Revisit the recalibration algorithm

Recalibrate on a restricted concentration range OR within the measurement range

Revisit the calibration of your immunoassay (number of calibration points, range, and calibration function)

Investigate the stability of calibration in the low and high measurement range

Reconsider the measurement range

Exclude outliers which negatively influence the recalibration fit

Investigate stability and reproducibility of your assay

Agenda

Discussion items

- Phase IV method comparison studies for TSH & FT4
- **Reference interval studies**
- Preparation of implementation – Awareness/Support
- Way forward

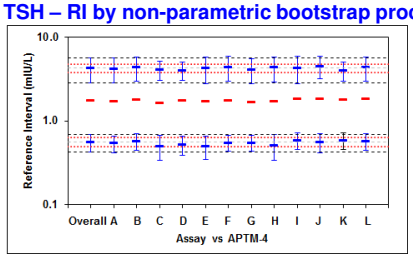
Reference interval studies

Characteristics of the 2 panels

		TSH RI	FT4 RI
Age (year)	Median	53	55
	Range	19-84	19-84
Gender	Female	59	58
	Male	61	62
Ethnicity	African American	16	10
	Caucasian	102	108
	Native American	0	1
	Hispanic	1	1
	Asian American	1	0
Medication	Yes	43	60
	No	77	57
	Unknown		3
Smoker	Yes	37	24
	No	83	96
Body Mass Index	Median	29	29
	Range	20-49	14-55
TSH screening	Median	1.9 mIU/L	1.8 mIU/L
	Range	0.5-6.8 mIU/L	0.5-6.8 mIU/L

Reference interval studies

TSH – RI by non-parametric bootstrap procedure



"Overall" RI
Median: 1.77 mIU/L
Width: 3.72 mIU/L

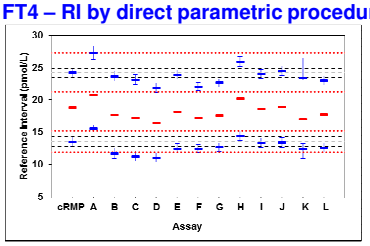
Lower limit (90% CI):
0.56 mIU/L
(0.42 – 0.69 mIU/L)

Upper limit (90% CI):
4.29 mIU/L
(2.85 – 5.72 mIU/L)

→ Outcome very nice (2.5 and 97.5 percentiles of all IAs within the CI around the "overall" percentiles)
→ Use of common RIs justified

Reference interval studies

FT4 – RI by direct parametric procedure (apart from 1 IA)



ED-ID/MS RI
Mean: 18.9 pmol/L
Width: 10.7 pmol/L

Lower limit (90% CI):
13.5 pmol/L
(12.8 – 14.2 pmol/L)

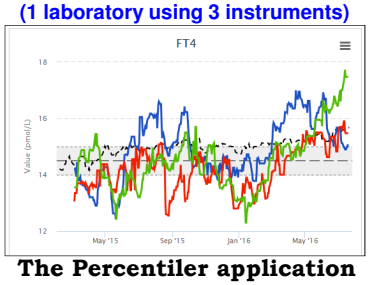
Upper limit (90% CI):
24.3 pmol/L
(23.6 – 25.8 pmol/L)

→ Outcome reasonable (2.5 and 97.5 percentiles of most IAs within a limit of ±12.5% (---) around those by ED-ID/MS)

→ Confounding factors: quality of calibration procedures, variability/instability of reagents and calibration lots, lot-to-lot differences, other?

Confounding factors in RI studies

Example of instability of one of the FT4 assays
(1 laboratory using 3 instruments)

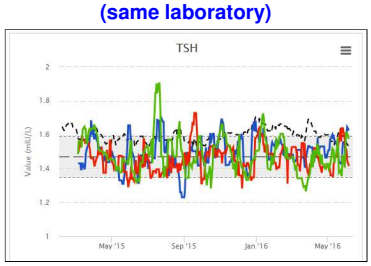


The Percentiler application

EMPOWER IVD GLOBE

Confounding factors in RI studies

In contrast, observe the stability of theTSH assay
(same laboratory)



The Percentiler application

EMPOWER IVD GLOBE

Agenda

Discussion items

- Phase IV method comparison studies for TSH & FT4
- Reference interval studies
- **Preparation of implementation – Awareness/Support**
- Way forward

Preparation of implementation

Benefit/risk analysis
By LM Thienpont, JD Faix, and G Beastall

"Standardization of Free Thyroxine and Harmonization of Thyrotropin Measurements: A Request for Input from Endocrinologists and Other Physicians/Patients."

1. Thyroid 2015;25:1379-80.
2. Clin Endocrinol (Oxf) 2015 Jul 23. [Epub ahead of print]. Endocr J 2015;62:855-6.
3. Exp Clin Endocrinol Diabetes 2016;124:61-2.
4. Endocrine 2015;50:826-7.
5. Eur Thyroid J 2015;4:217-2.
6. Endocr Pract 2016;22:374.
7. AACC Endocrinology Division Newsletter 2016; vol 2: issue 1.
8. ThyroWorld Volume 18 Summer 2015; 13-4.

Preparation of implementation

Create awareness
By JB Faix

Paper on TSH harmonization in preparation

"Thyroid International" (ISSN 0946-5464)
publication series published by Merck Serono (division of Merck KGaA).

These papers are written by renowned international thyroid experts in order to pass on the extensive experience which the authors possess in their fields to a wide range of physicians dealing with the diagnosis and therapy of thyroid

Preparation of implementation

Create awareness
By JB Faix, and LM Thienpont

Paper in preparation (on invitation)

"Advances in the Diagnosis and Management of Thyroid Disorders Using Laboratory Testing."

"Critical Reviews in Clinical Laboratory Sciences"

Awareness/Support

American Thyroid Association (ATA)
Contacted on behalf of C-STFT by JB Faix
➔ Letter of support (in: June 30, 2016)

Antonio Bianco, MD, PhD
ATA President

AMERICAN THYROID ASSOCIATION
FOUNDED 1923
2015-2016
President
Antonio Bianco, M.D., Ph.D. (2015-2016)
Chicago, Illinois

Victor Bernet, MD
ATA Secretary/COO

Stefan Grebe, MD, PhD, FRACP
Chair, ATA Laboratory Services Committee

Awareness/Support

ATA
Letter of support (June 30, 2016)

"This is with regards to your original inquiry … regarding ATA support for the IFCC's thyroid function testing harmonization efforts.

We support these efforts and are happy to assist you in every reasonable way. We note that our association's journal Thyroid has recently printed your letter. Please let us know which concrete measures you feel are suitable for our collaboration and assistance".

american thyroid association

Awareness/Support

European Thyroid Association (ETA)
Secretary of ETA, Prof. C. Dayan (Cardiff University), contacted by G Beastall

"Executive Committee agreed this is an important initiative of wide relevance. They suggested that the best way forward would be to put together an outline paper on this important work which they would then submit to the Guidelines subcommittee of the ETA (chair: Prof Pacini). It would be the hope that this would then develop into an approved ETA guideline formerly approved by the subcommittee and the ETA".

ETA European THYROID Association

Awareness

Two new IVD companies recently joined after they had been contacted by Dr. A. Hishinuma

- **SYSMEX Corporation (Kobe, JP)**
- **LSI Medience Corporation (Chiyoda-ku Tokyo, JP)**

➔ Familiarization study successfully completed; report sent
➔ Will soon measure the Phase IV panels for FT4 and TSH (deadline end of August)
➔ Will do the recalibration
➔ Will measure the reference interval panels

Agenda

Discussion items

- Phase IV method comparison studies for TSH & FT4
- Reference interval studies
- Preparation of implementation – Awareness/Support
- **Way forward**

Way forward – Question 1

TSH

RI study demonstrated success of technical recalibration (= proof-of-concept), hence:

Can we agree on preparing the implementation of the harmonized TSH assays?

- Can each IVD-company representative on the C-STFT obtain a formal agreement of his/her management?
- What timelines are feasible?

Way forward – Question 2

FT4

Outcome of RI study reasonable, but:

Do manufacturers agree that improvement of their assays (quality of calibration procedures, variability/instability of reagents and calibration lots, …) may be needed before implementation?
NOTE: collaboration of UGent with 2nd reference lab expected soon

- What timelines are feasible?

Way forward – Question 3

TSH implementation

How will IVD-companies prepare for the new 510k clearance of their harmonized assays, provided this will be required?

- What is the advice from the FDA?
- What timelines are feasible for final implementation?

Way forward – Question 4

Further role of the C-STFT

Do manufacturers agree with the following role/plans?

- Write 2 manuscripts on the Phase IV and reference interval studies (submit to "Clin Chem")
- Prepare new IVD companies for joining: Guide them through the familiarization-, technical recalibration phase and RI studies
- Continue the stability study of the panels
- Publish the process of benefit-risk analysis?

Note: last financing (8,000 CHF) for the scientific secretary 2016-'17

Way forward – Question 5

Further role of the C-STFT to assess/prove the sustainability of the FT4/TSH "standardization/ harmonization" status

Tool available; are IVD-companies prepared to collaborate and use it?

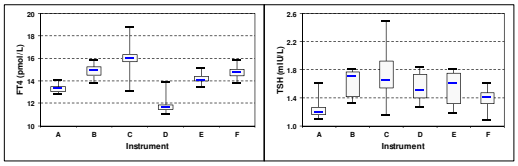
The Percentiler application

EMPOWER IVD GLOBE

De Grande LA, Goossens K, Van Uytfanghe K, Das B, MacKenzie F, Patru MM, Thienpont LM; IFCC Committee for Standardization of Thyroid Function Tests (C-STFT). Monitoring the stability of the standardization status of FT4 and TSH assays by use of daily outpatient medians and flagging frequencies. Clin Chim Acta 2016 Apr 27. pi: S0009-8981(16)30157-7. doi: 10.1016/j.cca.2016.04.032 [Epub ahead of print]

Way forward – Question 5

FT4/TSH: Comparison between manufacturers from patient medians ("pre-standardization/harmonization phase")

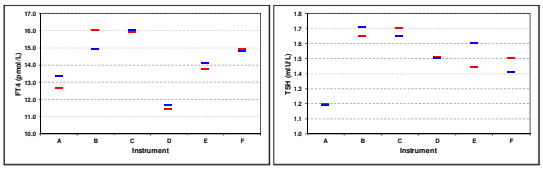


The Percentiler application

EMPOWER IVD GLOBE

Way forward – Question 5

FT4/TSH: Percentiler patient medians compare well with the standardization status observed in the Phase I method comparison



The Percentiler application

EMPOWER IVD GLOBE

Way forward – Question 6