

## Biennial activity report from JCTLM Member organizations

**Organization: Ref4U – Laboratory for Toxicology – Ghent University**

**JCTLM Member status:** Stakeholder Member

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**Period covered:** 2015 – 2017

### 1. Major achievements in support of standardization in laboratory medicine

Ref4U continues the activities of the former Laboratory for Analytical Chemistry at Ghent University, led by Professor Emeritus Linda Thienpont ([see publications](#)). All these activities support the efforts to develop and implement a measurement infrastructure for SI-traceable "measurands" in Laboratory Medicine (EN/ISO 17511).

Ref4U, as a reference laboratory, has expertise in conducting SI-traceable reference measurement procedures, listed in the database of the "Joint Committee for Traceability in Laboratory Medicine (JCTLM)". It offers services to the In Vitro Diagnostic industry, metrological institutes, organizers of external quality assessment and other interested parties. An overview of these services, including the associated reference measurement procedures, is given in the JCTLM database. For these measurement services Ref4U is accredited by BELAC (ISO 17025 and ISO 15195), see also the certificate with accompanying scope.

Additional research activities are focused on developing, validating and applying accuracy-based (SI-traceable) reference measurement procedures for substrates, metabolites, total and free steroid and thyroid hormones, 25 hydroxyvitamin D, peptides and proteins in serum. All reference measurement procedures are based on isotope dilution – mass spectrometry, in combination with extensive sample preparation procedures. Further interests of Ref4U are statistical and graphical techniques for the interpretation of method validation and method comparison.

Ref4U is as reference laboratory involved in the activities of the Committee for Standardization of Thyroid Function Tests (C-STFT). The mission statement of the C-STFT is to document and improve the standardization status and intrinsic quality of current thyroid hormone immunoassays. One of the tasks was to develop reference measurement systems for the most commonly determined thyroid hormones (TT4, TT3, FT4, FT3 and TSH). After a first method comparison study to document the state-of-the-art of the TSH and FT4 measurements, the C-STFT focused on the harmonization of TSH assays and the standardization of FT4 assays. During the last two years the focus of Ref4U within this project was to certify the reference materials to be used for standardization of FT4 immunoassays. Hence, 3 separate panels, the FT4 standardization panel, the reference interval panel and the first follow-up panel were measured in the reference laboratory with the FT4 reference measurement procedure<sup>1-4</sup>. All of this is described in more detail in a Clin Chem manuscript by De Grande LAC et al. listed below under 3.

## 2. Planned activities in support of standardization in laboratory medicine

The focus of the activities of Ref4U with regard to standardization in laboratory medicine will be on:

1. A continuation of the previous mentioned activities within the C-STFT. In this regard, the main focus will be on the development of a network of reference laboratories for FT4 (see also under 4).
2. Providing reference measurement services to the in-vitro diagnostic industry.

Ref4U also aims to further develop and validate candidate reference measurement procedures for SI-traceable measurands.

## 3. Promoting traceability in laboratory medicine

Traceability has been promoted in several ways during the last two years. Below a list of publications, poster and oral presentations.

### Publications

- Thienpont LM, Faix JD and Beastall G. Standardization of FT4 and harmonization of TSH measurements - a request for input from endocrinologists and other physicians. Clin Endocrinol 2016;84:305-6.
- Thienpont LM, Faix JD and Beastall G. Standardization of FT4 and harmonization of TSH measurements - A request for input from endocrinologists and other physicians. Exp Clin Endocrinol Diabet 2016;124:61-2.
- Thienpont LM, Faix JD and Beastall G. Standardization of FT4 and harmonization of TSH measurements: a request for input from endocrinologists and other physicians. Endocrine 2015;50:826-7.
- Thienpont LM, Faix JD and Beastall G. Standardization of free thyroxine and harmonization of thyrotropin measurements: A request for input from endocrinologists and other physicians. Thyroid 2015;25:1379-80.
- Thienpont LM, Faix JD and Beastall G. Standardization of FT4 and harmonization of TSH measurements - a request for input from endocrinologists and other physicians. Endocr J 2015;62:855-6.
- Thienpont LM, Faix JD and Beastall G. Standardization of FT4 and harmonization of TSH measurements - a request for input from endocrinologists and other physicians. Endocr Pract 2016;22:374.
- Thienpont LM, Faix JD and Beastall G. Standardization of Free T4 and harmonization of TSH measurements: A request for input from endocrinologists and other physicians. Eur Thyroid J 2015;4:271-2.
- Thienpont L, Faix J and Beastall G. Inquiry: Standardization of thyroid tests. The future standardization of FT4 and harmonization of TSH measurements in serum. A request for input on benefits and risks from Thyroid Foundations. ThyroWorld Newsletter 2015:13-4.
- 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 2017;467:4-18.

- Thienpont LM, Van Uytfanghe K, De Grande LAC, Reynders D, Das B, Faix JD, MacKenzie F, Decallonne B, Hishinuma A, Lapauw B, Taelman P, Van Crombrugge P, Van den Bruel A, Velkeniers B, Williams P on behalf for the IFCC Committee for Standardization of Thyroid Function Tests (C-STFT). Harmonization of serum thyroid-stimulating hormone measurements paves the way for the adoption of a common reference interval. Clin Chem 2017;63:1248-60.
- De Grande LAC, Van Uytfanghe K, Reynders D, Das B, Faix JD, MacKenzie F, Decallonne B, Hishinuma A, Lapauw B, Taelman P, Van Crombrugge P, Van den Bruel A, Velkeniers B, Williams P, Thienpont LM on behalf for the IFCC Committee for Standardization of Thyroid Function Tests (C-STFT). Standardization of free thyroxine measurements paves the way for the adoption of a more uniform reference interval. Clin Chem 2017;63:1642-52.

#### Poster presentations

- De Grande LAC, Goossens K, Van Uytfanghe K, Thienpont LM. Monitoring of the standardization and harmonization status of FT4 and TSH assays by use of patient medians. AACC Annual Scientific Meeting, 31 July - 4 August 2016, Philadelphia, PA, USA.
- De Grande LAC, Reynders D, Van Uytfanghe K, Thienpont LM on behalf of C-STFT. Harmonization of serum thyroid-stimulating hormone by the IFCC Committee for Standardization of Thyroid Function Tests (C-STFT) makes the use of a common reference interval possible. IFCC-EFLM EuroMedLab, 11-15 June 2017, Athens, Greece.

#### Oral presentations

- Progress in Standardization of Thyroid Function Tests. Dr. Katleen Van Uytfanghe. UZ Leuven, Belgium, January 2015.
- Progress in Standardization of Thyroid Function Tests. Dr. Katleen Van Uytfanghe. XXII Congreso Latinoamericano de Bioquímica Clínica y Ciencias de Laboratorio, COLABIOCLI - 2015, held in Quito, 24 - 26 September 2015.
- International Standardization of the Thyroid Markers Free T4 and TSH. Prof. Dr. Linda Thienpont. 9e Symposium bioclinique de la SFMN, Paris, France. 15 - 16 October 2015.
- Progress in Standardization of Thyroid Function Tests. Dr. Katleen Van Uytfanghe. Protein and Peptide Therapeutics and Diagnostics: Research and Quality Assurance' workshop, Chengdu, China. 1 - 3 June 2016.
- Standardization of Thyroid Function Tests. Dr. Katleen Van Uytfanghe. Calilab 2016, Buenos Aires, Argentina. 30 November - 2 December 2016.

#### **4. Reference laboratory networks/collaborations focusing on developing /implementing reference measurement systems**

Ref4U yearly participates in the IFCC External Quality Assessment Scheme for calibration laboratories in clinical chemistry (RELA). In 2015 we successfully participated for 25-hydroxyvitamin D, estradiol, testosterone, TT3 and TT4 and in 2016 for 25-hydroxyvitamin D, estradiol, progesterone, cortisol and TT4. In 2017 we subscribed to participate for

testosterone, TT3 and TT4. Our aim is to participate for the analytes in our scope, at least once every three years.

Next to that Ref4U takes the lead within the C-STFT with regard to establishing of a network of competent reference laboratories for FT4 in the framework of the activities of the C-STFT. As coordinator we have so far solicited three laboratories (some with expertise in reference measurement services) to become a partner in the FT4 Reference Laboratory Network (RLN), these are: the Centers for Disease Control and Prevention (CDC, Atlanta, USA), the Reference Material Institute for Clinical Chemistry Standards (ReCCS, Japan) and the Radboud University Medical Center of Nijmegen (Nijmegen, the Netherlands). The network members are currently developing/revalidating their FT4 RMPs, were after a first method comparison will be organized.

## **5. Open questions and suggestions to be addressed by JCTLM**

## **6. References**

<sup>1</sup> Van Houcke SK, Van Uytfanghe K, Shimizu E, Tani W, Umemoto M, Thienpont LM, International Federation of Clinical Chemistry and Laboratory Medicine Working Group for Standardization of Thyroid Function Tests. IFCC international conventional reference procedure for the measurement of free thyroxine in serum: International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) Working Group for Standardization of Thyroid Function Tests (WG-STFT)(1). Clin Chem Lab Med 2011;49:1275-81.

<sup>2</sup> Van Uytfanghe K, Stöckl D, Ross HA, Thienpont LM. Use of frozen sera for FT4 standardization: investigation by equilibrium dialysis combined with isotope dilution-mass spectrometry and immunoassay. Clin Chem 2006;52:1817-21.

<sup>3</sup> International Federation of Clinical Chemistry and Laboratory Medicine IFCC, IFCC Scientific Division Working Group for Standardization of Thyroid Function Tests WG-STFT, Thienpont LM, Beastall G, Christofides ND, Faix JD, Ieiri T, Jarrige V et al. Proposal of a candidate international conventional reference measurement procedure for free thyroxine in serum. Clin Chem Lab Med 2007;45:934-6.

<sup>4</sup> Thienpont LM, Beastall G, Christofides ND, Faix JD, Ieiri T, Miller WG et al.; International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) IFCC Scientific Division Working Group for Standardization of Thyroid Function Tests (WG-STFT). Measurement of free thyroxine in laboratory medicine—proposal of measurand definition. Clin Chem Lab Med 2007;45:563-4.