

Biennial activity report from JCTLM Member organizations

All JCTLM Members are invited to attend the Members' and Stakeholders' Meeting, which is held once every two years, and submit a report of their activities in support of traceability in laboratory medicine over the preceding period.

For that purpose this template document provides guidance to JCTLM Members for drafting their biennial activity report. Organizations are invited to provide the information below for submission to the Executive Committee.

Organization Name: Ref4U – Laboratory for Toxicology – Ghent University

JCTLM Member status: Stakeholder Member

Author(s): Katleen Van Uytfanghe

Author(s) email(s): katleen.vanuuytfanghe@ugent.be

Period covered: 2022 – 2023

1. Major achievement(s) in support of standardization in laboratory medicine

Ref4U's 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, conducts SI-traceable reference measurement procedures as 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](#).

Ref4U, by representation of Dr. Van Uytfanghe, is active as a partner in the [EMN on Traceability in Laboratory Medicine](#), the [JCTLM task force on reference measurement system implementation](#) and the ATA Thyroid Function Tests Writing Group. Ref4U, by representation of Dr. Van Uytfanghe, co-authored 2 projects in the framework of Euramet's European Partnership on Metrology - Call 2022 and 2023.

Ref4U is as reference laboratory very actively involved in the activities of the IFCC 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). Activities are now focused on the implementation of these reference measurement systems: (i) by establishing a network of FT4 reference laboratories; (ii) by ensuring sustainability of TSH harmonization; (iii) by dissemination of the work of the C-STFT so that new research (e.g. in establishing regional reference intervals) will be linked to the standards set by the C-STFT; (iv) supporting IVD manufacturers in implementing the standardized FT4 and harmonized TSH assays. Ref4U supports activities of other IFCC working groups/committees as well by means of providing reference measurement services or as a corresponding member. This work resulted in several joint publications, see section 3.

Additional research activities are focused on the **implementation of the principles of standardization** beyond the field of clinical chemistry, more particular **in the field of toxicology**, with current focus on the measurement of the direct alcohol biomarker phosphatidylethanol. In the framework of these activities a workshop was held at [The 2022 PEth in Mind Conference - PEth-NET](#), discussing the future road towards comparability of phosphatidylethanol measurement results. The latter resulted in the publication of a [consensus](#) statement in which the measurand "phosphatidylethanol" is now defined.

2. Planned activity(ies) 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.
2. Providing reference measurement services to the in-vitro diagnostic industry, and other interested parties.
3. Ref4U also aims to further develop and validate candidate reference measurement procedures for SI-traceable measurands.
4. Ref4U will continue to promote standardization in the field of toxicology.
5. Ref4U will continue its activities within the EMN on Traceability in Laboratory Medicine.
6. Ref4U will continue its activities within the JCTLM task force on reference measurement system implementation

3. Promoting traceability in laboratory medicine

Publications

1. Van Uytfanghe K, Ehrenkranz J, Halsall D, Hoff K, Loh TP, Spencer CA, Köhrle, J. Thyroid Stimulating Hormone and Thyroid Hormones (Triiodothyronine and Thyroxine): An American Thyroid Association-Commissioned Review of Current Clinical and Laboratory Status. *Thyroid*. 2023 Sep;33(9):1013-1028. doi:10.1089/thy.2023.0169
2. Loh TP, Ehrenkranz J, Halsall D, Spencer CA, Van Uytfanghe K, Köhrle J. Clinical Interpretation of Thyroid Tests: Considerations for Reference Intervals. *Thyroid*. 2023 Apr;33(4):404-406. doi:10.1089/thy.2023.0096
3. Ribera A, Zhang L, Ribeiro C, Vazquez N, Thonkulpitak J, Botelho JC, Danilenko U, van Uytfanghe K, Vesper HW. Practical considerations for accurate determination of free thyroxine by equilibrium dialysis. *J Mass Spectrom Adv Clin Lab*. 2023 Jun 23;29:9-15. doi:10.1016/j.jmsacl.2023.06.001
4. Jansen HI, van der Steen R, Brandt A, Olthaar AJ, Vesper HW, Shimizu E, Heijboer AC, Van Uytfanghe K, van Herwaarden AE. Description and validation of an equilibrium dialysis ID-LC-MS/MS candidate reference measurement procedure for free thyroxine in human serum. *Clin Chem Lab Med*. 2023 Mar 31;61(9):1605-1611. doi:10.1515/ccclm-2022-1134
5. Ribera A, Zhang L, Dabbs-Brown A, Sugahara O, Poynter K, van Uytfanghe K, Shimizu E, van Herwaarden AE, Botelho JC, Danilenko U, Vesper HW. Development of an equilibrium dialysis ID-UPLC-MS/MS candidate reference measurement procedure for free thyroxine in human serum. *Clin Biochem*. 2023 Jun;116:42-51. doi:10.1016/j.clinbiochem.2023.03.010
6. Cowper B, Partridge K, Rigsby P, Lyle A, Vesper H, Van Uytfanghe K, Burns C. 4th WHO International Standard for thyroid-stimulating hormone (TSH), human, pituitary. WHO/BS/2023.2454
7. Luginbühl, M, Van Uytfanghe, K, Stöth, F, Wurst, FM, & Stove, CP. Current evolutions, applications, and challenges of phosphatidylethanol analysis for clinical and forensic purposes. *WIREs Forensic Science*, 4(5), e1456. doi:10.1002/wfs2.1456
8. Luginbühl M, Wurst FM, Stöth F, Weinmann W, Stove CP, Van Uytfanghe K. Consensus for the use of the alcohol biomarker phosphatidylethanol (PEth) for the assessment of abstinence and alcohol consumption in clinical and forensic practice (2022 Consensus of Basel). *Drug Test Anal*. 2022 Oct;14(10):1800-1802. doi:10.1002/dta.3340

Presentations

1. Keynote lecture – “Increasing the confidence in phosphatidylethanol measurements – The road to comparability of results over time, location and assay”. The 2022 PEth in Mind Conference, 19-20 May 2022, Basel, Switzerland
2. Reference systems for thyroid functions tests (the IFCC standardization committee). European Thyroid Association - Clinical & Scientific Update 2022, 10-13 September 2022, Brussel
3. Presentation in Dutch on the standardisation of thyroid function tests: “Standaardisatie Schildklierdiagnostiek. Post Academisch Onderwijs Klinische Chemie schildklier”, Dutch Society of Clinical Chemistry and Laboratory Medicine, 23 June 2022, virtual

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

- Ref4U is a partner in the FT4 Reference Laboratory Network (RLN), established under the auspices of the C-STFT. Other members 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).

5. Open questions and suggestions to be addressed by JCTLM

Note: The information of this report will be accessible publicly on the relevant JCTLM Members webpage, unless the author of the report states otherwise. In the case the organization does not authorize the publication of the report in part or full, the author will add a statement to clarify which part(s) of the report will /will not be rendered public.