From: Linda Thienpont, PhD

Date: October 22, 2007

Ref: Project proposal

IFCC WG on Standardization of Thyroid Function Tests (WG-STFT)
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Re: Project proposal: Method comparison of free T4 immuno- and routine MS assays with the candidate international conventional reference measurement procedure based on ED ID-LC/Tandem MS

Dear Colleagues,

In the last open meeting of the WG-STFT with IVD-industry and other parties with an interest in thyroid function tests (July 16th 2007, San Diego, AACC Annual Conference), we have proposed to organize a pilot method comparison study of free T4 routine assays (immuno- and MS assays) with the candidate international conventional reference measurement procedure based on Equilibrium Dialysis Isotope Dilution-Liquid Chromatography/Tandem Mass Spectrometry (ED ID-LC/Tandem MS). The objective of this study should be to assess the standardization needs and the potential for assay harmonization.

As explained in the meeting, IFCC does not fund such projects but requires the finance to be raised by subscription/contribution from interested parties. The cost of participation of an IVD-manufacturer in the project will be max. 9,500 EURO (note: this amount is calculated from dividing the total cost of the project, i.e. 95,000 EURO, by 10 (in the supposition that at least 10 manufacturers will participate; if there are more participants, the charge per manufacturer will proportionally decrease). The cost for participation of a routine MS laboratory has been fixed at 1,500 EURO.

It has been suggested in the meeting by you that you would like to receive an outline of the project in order to allow you to properly discuss it within your company/laboratory/organization. It is with pleasure that we send you the outline today (see annex 1).

We hope that it is obvious that before we can start, we need a **definite** answer as to whether you will participate in this project or not. A reply form is added in annex 2. We would very much appreciate if you would **E-MAIL your reply** to **linda.thienpont@ugent.be** **by the 8th of December**. Further details about the start of the project (planned in the spring of 2008) will be sent in due time to those colleagues who have expressed an interest in participating.

Last but not least, we have pleasure in informing you that meanwhile the representatives of the Thyroid Associations (TAs) in our WG made progress with regard to defining the clinical need for standardization of free T4 measurements. We received in this context a letter from the President of the British TA (see annex 3). Also the President Elect of the Japan TA informed our WG that in Japan they took the decision to standardize free T4 measurements in 2008 (statement made at Euromedlab 2007, June 4th 2007). We also have been informed that the European TA formalized in its General Assembly 2007 a Clinical WG on Standardization, and that the Board of Directors and the Laboratory Services Committee of the American TA is preparing a letter of support.

Looking forward to hearing from you,
with best wishes,
Linda Thienpont, Chair

on behalf of all members of the IFCC WG-STFT

Annex 1

IFCC WG on Standardization of Thyroid Function Tests (WG-STFT)

Project proposal: Method comparison study of free T4 assays with the candidate international conventional reference measurement procedure based on Equilibrium Dialysis Isotope Dilution-Liquid Chromatography/Tandem Mass Spectrometry (ED ID-LC/Tandem MS)[1] – Assessment of standardization needs and potential for assay harmonization

Materials
- 40 single-donation sera prepared by the CLSI C37-A protocol[2], without filtration.
- Prepared by Solomon Park Research Laboratories (Kirkland, WA 98034, USA).
- Storage: not longer than 3 months at -70°C.
- Delivery form: 3 x 1 mL of each serum = 3 sets of 40 sera.
- Selection criteria: serum TSH, TBG and total proteins.
- Negative in testing for infectious diseases: HIV, HbsAg, HCV, RPR.

Reference measurement procedure
Value assignment by UGent with the ED ID-LC/Tandem MS procedure[3], 4 independent measurements with control of 10 samples by a 2nd laboratory: HECTEF (Standard Reference Center Foundation, Kawasaki-City, Kanagawa 213-0012, Japan).

Routine assays for free T4
- From IVD-manufacturers.
- From laboratories offering ED or UF ID-LC/Tandem MS routine services.
- Will receive 3 sets of 40 sera.
- Are requested to:
    - perform triplicate measurements in 1 run.
    - Control the measurements by doing “intensive” quality control with own IQC materials (e.g.: 3 IQC-materials; measurement in triplicate at the start, mid, and end of run: n = 9 for each material).
    - Document individual measurement results in an EXCEL-report form prepared and sent beforehand by UGent.
    - Report data to UGent (linda.thienpont@ugent.be).

Added value from the study for participants
Besides method comparison of their routine assay with ED ID-LC/Tandem MS, the study will offer the possibility to assign values to manufacturers/laboratories' own pools, intended for long-term quality assurance purposes, by measurement of the pools in parallel to the 40 single-donation sera. These values are intended for internal use, only and, hence, will be managed by manufacturers/laboratories themselves (will not be reported in the study).

Data treatment, presentation, and use (follow-up)
- Data will be treated and presented in a confidential and anonymous way.
- Data will be presented to the participants, preferably in conjunction with an international meeting (for example AACC 2008).
- The follow-up will be decided by the IVD-manufacturers/laboratories themselves.

Costs

- Total costs (sera; value assignment; logistics; data treatment): 95,000 EURO.
- Anticipated number of participants: at least 10.
- Cost per participating IVD-manufacturer: **maximum** 9,500 EURO (max. because calculated on the basis of 10 participants; if there are more, the charge will decrease proportionally).
- Cost per participating laboratory: 1,500 EURO (fixed).
- Project will not be initiated when the number of manufacturers is <10.

Project timeline

- Invitation letter: October 2007.
- Confirmation letter by IVD-manufacturers/routine laboratories: December 8, 2007.
- Project start: spring 2008.

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[1] Thienpont LM, Beastall G, Christofides ND, Faix JD, Ieiri T, Jarrige V, Miller WG, Miller R, Nelson JC, Ronin C, Ross HA, , Rottmann M, Thijssen JH, Toussaint B. Proposal of a candidate international conventional reference measurement procedure for free thyroxine in serum. Clin Chem Lab Med 2007;45:934-6.

[2]CLSI (formerly NCCLS). Preparation and Validation of Commutable Frozen Human Serum Pools as Secondary Reference Materials for Cholesterol Measurement Procedures; Approved Guideline. CLSI document C37-A (ISBN 1-56238-392-2). CLSI, 940 West Valley Road, Suite 1400, Wayne, Pennsylvania 19087-1898 USA, 1999.

[3]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.

Annex 2

Date

E-mail

FROM:

«Title» «FirstName» «LastName»
«Company»
«Laboratory»
«Address1»
«Address2»
«City» «PostalCode»
«Country»

Phone
E-mail

TO:

Prof. Dr. Linda Thienpont
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Please fill in and e-mail this form by the 8th of December 2007 at the latest to Linda.thienpont@ugent.be. Very many thanks.

My company/laboratory subscribes for the free T4 method comparison study and will financially contribute to receive 3 sets of 40 sera with free T4 values assigned by ED ID-LC/Tandem MS [Cost for an IVD-manufacturer ***maximum*** 9,500 EURO, cf. Annex 1] [Cost for a routine MS laboratory, 1,500 EURO]	YES ☐	NO ☐