



## en, a new kit for Calcitonin determination.

**Introduction:** Calcitonin, a 32 aminoacid peptide produced by the parafollicular C cells of the thyroid is the classical clinical marker for medullary thyroid carcinoma (MCT). In clinical practice, a patient with calcitonin concentration  $>10$  ng/L should undergo a pentagastrin test to exclude MCT. It is important to note, however, that these interpretive guidelines have been developed using the Cisbio international reagent set for calcitonin measurement. Recently, DiaSorin launched an improved version of the Liaison Calcitonin kit. The aim of that work was to evaluate this new kit.

**Material and methods:** We evaluated the precision with a modified protocol based on CLSI EP-5A2: 14 serum pools were assayed in six replicates per day on five different days. Linearity was evaluated based on CLSI EP-6A. We established the limit of quantification (for a total error of 20%), measurement uncertainty and the accuracy profile of the method. We evaluated the reference range in a healthy population (122 women and 145 men), selected on basis of the absence of anti-thyroglobulin antibodies, and normal levels of TSH and fT4. We studied the fidelity to the 2<sup>nd</sup> IS 89/620. With samples enriched with high amounts of this IS, we tried to observe if hook and carryover effects occurred. We studied the susceptibility of HAMA interference with selected samples, known to present an interference and finally, we compared the results with Cisbio on 267 consecutive and 45 samples obtained after pentagastrin stimulation.

**Results:** The LOQ was established at 5.3 ng/L. Repeatability and intermediate precision were  $<10\%$  in the studied range (2.9-1159 ng/L). The method was found to be linear until the 1/10 dilution. The kit was correctly calibrated against the IS, 1 $\mu$ UI corresponding to 5.5pg of Calcitonin Liaison (expected: 4.8-5.7 pg). Measurement uncertainty ranged from 25% at 2.9 ng/L to 6.5% at 1159 ng/L. The accuracy profile built with the predictive tolerance interval method shows that, on average, 95% of the future results that will be generated by this method will be included in the computed tolerance intervals of  $\pm 20\%$  in the 5.3-1159 ng/L studied range. Ninety-five percent of the healthy male and female presented calcitonin levels  $<10$  ng/L. We did not observe any hook effect with samples presenting values up to 1million ng/L, but there was a slight carry-over, with a blank sample giving an amount of 8 ng/L after being assayed after the 1million pg/L sample. Samples presenting spurious high levels due to HAMA interference with the 1<sup>st</sup> generation kit unfortunately gave the same erroneous profile. In the normal population, the Bland-Altman graph showed a mean difference of  $0.1 \pm 2.0$  ng/L between Liaison and Cisbio. In samples obtained after pentagastrin stimulation (range: 9.3-838 ng/L), the mean difference was  $11.1 \pm 49.3$  ng/L. No statistical difference was observed between the methods in these two populations.

**Conclusions:** Liaison Calcitonin II Gen is a very robust method. The analytical performances have greatly improved compared to the 1<sup>st</sup> version of the kit. The comparison with Cisbio is remarkable, which allows the use of the  $\approx 10$  ng/L cut-off for the screening of MCT.