THIS IS A SUMMARY OF AN ORTHO CLINICAL DIAGNOSTICS STUDY:

VITROS® Immunodiagnostic Products TSH3 Assay: Method Comparison with Six TSH Immunoassays

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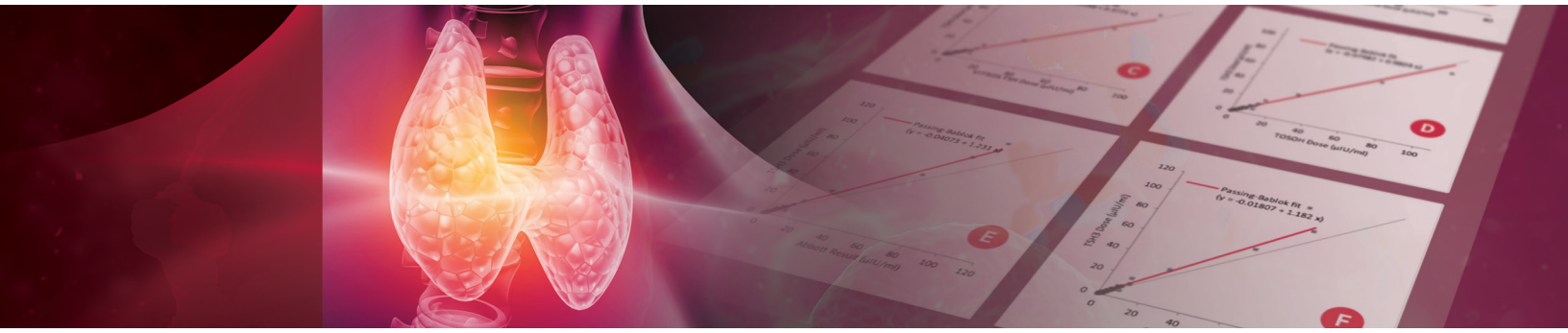


INTRODUCTION AND STUDY OBJECTIVE

Thyroid stimulating hormone (TSH) is a glycoprotein hormone synthesized and secreted from the pituitary gland, under the regulation of thyrotropin releasing hormone and thyroid hormones. It plays an important role in metabolic regulation.

TSH is guideline recommended first-line screening test for thyroid dysfunction, and is essential in the diagnosis and management of hyperthyroid and hypothryoid conditions.[1, 2, 3] Both the new VITROS TSH3 and current VITROS TSH assays meet the third-generation TSH assay definition which requires functional sensitivity of 0.01–0.02 µIU/mL (mU/L) and high precision to distinguish between mild and profoundly low TSH values seen with subclinical and overt hyperthyroidism.[4, 7, 8]

Improved Accuracy and Result Agreement were achieved by calibrating to the IFCC All Procedure Trimmed Mean panel (APTM-4) to minimize assay result variability.

VITROS TSH3 assay is calibrated to the IFCC All Procedure Trimmed Mean panel (APTM-4) to improve accuracy and agreement in comparison with other manufacturer TSH methods. As TSH is not a standardized assay, it can be challenging for clinicians to compare reference intervals and clinical cutoffs for instances where patients may receive care at various places or if network labs use multiple TSH methods. The World Health Organization International Reference Preparation (WHO IRP) for TSH is derived from human cadaver pituitary organs and may comprise glycosylated forms of TSH that differ from those typically present in serum TSH contributing to assay result variability.[5] A study by the IFCC Committee for Standardization of Thyroid Function Tests (C-STFT) demonstrated improved result agreement achieved by calibrating TSH assays to the APTM panel. The APTM panel values were statistically derived from patient split samples tested across multiple manufacturers.[6]

The objective of this study is to compare the VITROS TSH3 assay with six commercially available third-generation TSH assays using patient samples to evaluate result agreement.

METHOD

The following TSH assays were used in the evaluation: ADVIA Centaur® CP TSH3-Ultra (Siemens Healthcare Diagnostics), Elecsys TSH (Roche Diagnostics), ARCHITECT TSH (Abbott Diagnostics), Lumipulse TSH-III (Fujirebio), AIA-PACK® TSH (TOSOH), and VITROS TSH and VITROS TSH3 assay (Ortho Clinical Diagnostics)(Table 1).[7, 8, 9, 10, 11, 12, 13]

Table 1: Technical and analytical characteristics of the TSH assays used in this study, as quoted by the manufacturers

Method	Reference Interval	LOQ IU/mL (mIU/L	Traceability
VITROS TSH3	0.4001–4.049*	0.01	APTM-4
VITROS TSH	0.465–4.68	0.015	WHO IRP 80/588
Siemens	0.550–4.780	0.008	WHO IRP 81/565
Roche	0.270–4.20	0.014	WHO IRP 80/588
Abbott	0.47–4.64	0.012	WHO IRP 81/565
Fujirebio	0.464–3.728	0.02	WHO IRP 81/565
Tosoh	0.45–3.72	0.003	WHO IRP 81/565

Samples were purchased to span the common measuring range of the assays, with most samples falling within 0.0100–100.0 µIU/L. The samples were aliquoted, frozen and shipped to the testing sites on dry ice. They were tested with each of the immunoassays in singleton, according to the assay's package insert procedure, and quality controls run in accordance with the laboratory's practice.

VITROS TSH3 assay results were compared to the results from the six immunoassays used in this study. Passing-Bablok analysis of the data was performed with Analyze-it™ software (version 5.20). The correlation coefficient (r) were obtained from linear regression analysis using Analyze-it software. Kappa Statistic analysis was done by Excel.

* For euthyroid population

RESULTS AND DISCUSSION

Method Comparison

The comparability of VITROS TSH3 assay with the six TSH immunoassays was evaluated, using patient samples throughout the common measuring range of the TSH assays (Figure 1). The result linear regression and correlation coefficient are summarized in Table 2.

VITROS TSH3 assay demonstrated excellent result agreement with Siemens, Roche, Tosoh, and VITROS TSH assay methods.

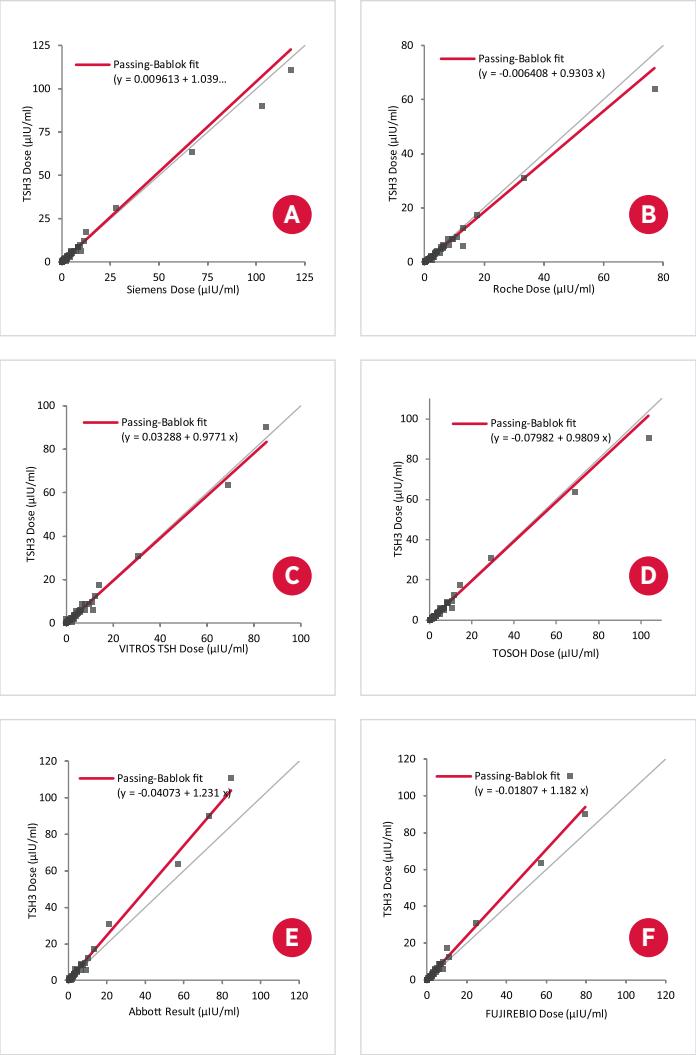
Comparisons to all six immunoassays demonstrate a very close correlation; Roche and Fujirebio had a Pearson's correlation coefficient of 0.99, while comparisons to all other assays had a correlation of 1.00. VITROS TSH3 assay agreed well with Siemens, Roche, Tosoh, and VITROS TSH assays, with slopes within 10% of 1.0. Slopes with the Abbott and Fujirebio were 1.23 and 1.18, respectively.

Table 2: Passing-Bablok linear regression and Pearson's correlation of VITROS TSH3 assay as compared with the different TSH immunoassays

Method	n	Passing-Bablok Linear Regression	Pearson's Correlation Coefficient (r)
VITROS TSH	46	y = 0.98x + 0.0329	1.00
Siemens	48	y = 1.04x + 0.0096	1.00
Roche	46	y = 0.93x – 0.0064	0.99
Abbott	48	y = 1.23x – 0.0407	1.00
Fujirebio	48	y = 1.18x – 0.0181	0.99
Tosoh	47	y = 0.98x – 0.0798	1.00

There was a relative positive bias of results for the VITROS TSH3 assay compared with Abbott and Fujirebio TSH assays, which was not unexpected as it is consistent with the data published in a recent IFCC harmonization study (*Harmonization of Serum Thyroid-Stimulating Hormone Measurements Paves the Way for the Adoption of a More Uniform Reference Interval*). This study demonstrated both Abbott and Fujirebio assays were negatively biased against APTM value in the IFCC patient panel intended to harmonize TSH assays. The median deviations were –7.0% to –14.0% for Abbott assay and –14.3% to –23.8% for Fujirebio assay, depending on the TSH levels evaluated.[6]

Figure 1: Passing-Bablok linear regression plots demonstrating method comparison of VITROS TSH3 assay as compared with six commercially available third-generation TSH immunoassays*



* The VITROS TSH3 method agreed well with Siemens, Roche, Tosoh, and VITROS TSH assays. Lack of agreement with the Abbott and Fujirebio methods was not unexpected based on a recent IFCC harmonization study.[6]

Clinical Concordance

TSH is not a standardized assay, and the clinical cutoffs are not harmonized either. Therefore, clinical correlation is more important when we compare two methods in practice. This is particularly important when a patient is seen in multiple facilities using different TSH assays.

Clinical concordance of VITROS TSH3 assay with comparative methods was determined. TSH concentrations below or above the lower or upper reference limits for each assay were used for diagnosing hyperthyroidism or hypothyroidism.

Among the populations studied, the percentage of samples diagnosed with hyperthyroidism was 15–20%, and the percentage of hypothyroidism samples was 27–40%, depending on different assays.

VITROS TSH3 assay demonstrated substantial to almost perfect clinical concordance with all six TSH immunoassays in this study, indicating good clinical accuracy for thyroid testing.

The agreement (kappa statistics) between VITROS TSH3 assay and the six TSH immunoassays at the diagnostic levels is shown in Table 3 and varied between 0.70 and 1.00 (all statistically significant, $p < 0.001$). VITROS TSH3 assay had almost perfect agreement (defined as Kappa = 0.81 ~ 1.00) with VITROS TSH assay, Siemens, Roche, Tosoh and Fujirebio TSH assays, and substantial agreement (defined as Kappa = 0.61 ~ 0.80) with the Abbott TSH assay.

Table 3: Agreement (kappa statistics and 95% CI) at the diagnostic threshold of VITROS TSH3 assay as compared with the different TSH immunoassays

Method	Cohens Kappa (95% CI)
VITROS TSH	0.90 (0.78–1.00)
Siemens	0.97 (0.90–1.00)
Roche	0.86 (0.73–0.99)
Abbott	0.70 (0.52–0.87)
Fujirebio	1 (1.00–1.00)
Tosoh	0.90 (0.79–1.00)

Although in the regression analysis, the slope between VITROS TSH3 assay and Fujirebio TSH assay is 1.18, above the acceptance criteria of 1.00 +/− 0.1, the clinical concordance study showed Cohens Kappa value between these two methods is 1.00. This can be attributed to the different diagnostic levels established by different immunoassays. VITROS TSH3 assay has the highest kappa value with both Siemens and Fujirebio, indicating excellent clinical concordance between them.

CONCLUSION

The new VITROS TSH3 assay demonstrated substantial to almost perfect clinical concordance with all six TSH immunoassays in this study, indicating good clinical accuracy for thyroid testing. Likewise, the method comparison study demonstrated good agreement between VITROS TSH3 assay and the other TSH assays.

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