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White Paper

Comparison and Evaluation of the Xprecia Stride Coagulation Analyzer to the Roche CoaguChek XS Coagulation System for Monitoring Oral Anticoagulant Therapy with Warfarin

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Introduction

Primary care, urgent care, and other point-of-care (POC) locations demand fast, reliable Prothrombin Time/International Normalized Ratio (PT/INR) test results to support the monitoring of oral anticoagulant therapy (OAT) with vitamin K antagonists such as warfarin.

The Xprecia Stride™ Coagulation Analyzer* from Siemens Healthcare is a novel, handheld POC device that generates rapid, quantitative PT/INR test results from fresh fingerstick blood. This external validation study, following ICH-GCP guidelines,† assessed the substantial clinical equivalence of the Xprecia Stride analyzer PT/INR test against a widely used FDA-cleared POC method (CoaguChek XS system, Roche Diagnostics).

Summary

Method comparison with the CoaguChek XS system validated Xprecia Stride analyzer performance according to its intended use with fingerstick blood samples across the 0.8–8.0 INR range. Xprecia Stride analyzer PT/INR test results demonstrated strong correlation with the CoaguChek XS system (r^2=0.94). Bias fell within limits of acceptance. Using a 2.0–4.0 INR therapeutic range, clinical concordance of results generated by the two POC methods was 97.0%.

Repeatability of Xprecia Stride analyzer PT/INR results (versus laboratory BCS® XP System measurement) was well within a ≤10% coefficient of variation (%CV), an industry-accepted criterion, across four reporting ranges (results yielding CVs of ≤5.8%). Assessment of two levels of liquid quality control (LQC) demonstrated intermediate precision well within this same industry standard (results yielding within-laboratory CVs of ≤7.0%).

The Increasing Demand for Oral Anticoagulant Therapy (OAT)

OAT is prescribed on a long-term basis for people who have experienced recurrent abnormal blood clotting or for those who are at high risk of developing clots. For example, patients with atrial fibrillation (also known as AF or AFib), a common cardiac arrhythmia that affects more than 6 million people in Europe and 2.6 million in the USA,[1] are at risk for blood clots, including those that cause ischemic stroke. OAT is frequently prescribed to reduce these stroke risks, but use of these medications typically necessitates frequent patient monitoring through blood tests.

More than 800 million PT/INR tests are conducted annually worldwide.[2] An increasing population of patients on warfarin (COUMADIN) therapy and the trend towards testing outside of the central laboratory have escalated the demand for PT/INR results at the point of care.

*Under FDA review. Not available for sale in the U.S. Product availability varies by country.

†Evaluation of Precision Performance of Quantitative Measurement Methods (EP05-A2), Measurement Procedure Comparison and Bias Estimation Using Patient Samples (EP09-A3), and Defining, Establishing, and Verifying Reference Intervals in the Clinical Laboratory (EP28-A3c). The concepts and information presented in this paper are based on research and are not commercially available.

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Xprecia Stride Analyzer: Clinical Utility

The Xprecia Stride analyzer is intended for near-patient monitoring of Prothrombin Time/ International Normalized Ratio (PT/INR) on fresh fingerstick blood samples. It is an accurate, convenient, easy-to-use handheld instrument with enhanced safety features designed to protect operators during the testing process:

- Easy-to-use color touchscreen interface and clear display of results as seconds (PT) or INR units.
- Fast, quantitative results across the 0.8–8.0 INR reportable range.
- Small, 6 µL sample size.
- Onboard animated tutorial demonstrates main functions and provides step-by-step pictorial prompts to guide users during operation.
- Pushbutton ejection of used test strips minimizes biohazard exposure.
- Integrated bar-code scanner facilitates error-free data capture.
- Seamless, secure bidirectional data transfer via USB connection.

Siemens Healthcare has been a market leader in laboratory hemostasis testing for more than 30 years and can now provide a POC solution for warfarin monitoring. The Xprecia Stride Coagulation Analyzer extends Siemens Healthcare's hemostasis expertise into the POC arena and gives customers the choice of a broad portfolio of hemostasis analyzers, all from the same manufacturer.

Xprecia Stride Analyzer: Test Technology

Siemens Healthcare's Xprecia Stride analyzer employs electrochemical technology and single-use reagent test strips to measure the prothrombin time. A sample chamber in the test strip is filled with the blood sample through capillary action.

The strip contains dried reagents consisting primarily of thromboplastin, an electroactive thrombin substrate, and other reagents. An electroactive group released from the thrombin substrate is detected electrochemically at the electrodes in the strip; the current produced is measured by the Xprecia Stride Analyzer to determine the coagulation time.
The analyzer performs two on-strip quality control checks each time a sample is applied to a test strip: to check for presence of adequate sample and reagent volume on the test strip and to check for test strip degradation due to exposure to environmental factors. If either control fails, the analyzer reports an error and cancels the test.

Operators may also use LQC material in accordance with local, state, federal, or national guidelines.

The Diversity of Coagulation Testing Platforms and Reagents

Commercially available analyzers used to perform PT/INR testing employ a variety of different reagents, including Dade® Innovin®, Thromborel® S, Owren's PT (combined thromboplastin), Stago STA Neoplastine CI Plus, and IL HemosIL RecombiPlasTin. Differences in reagents, instruments, and other variables can affect PT/INR results and increase the complexity of method performance comparisons.

This study assessed results reported by platforms that use the same test reagent (Dade Innovin recombinant human tissue thromboplastin), removing a potential area for variability when comparing the two methods.

The Importance of Clinical Concordance

INR clinical concordance is essential in order to make reliable patient treatment decisions, particularly when decisions rely on newly introduced analytical methodology. Not all methods used to measure a prothrombin time will generate results that match. Although the INR helps to standardize interpretation of PT test results, there are still differences between methods, and reference ranges can vary between clinical contexts and sites.

Clinical concordance analysis provides an assessment of method agreement with respect to patient management decisions, which is particularly useful when results cannot be compared directly. This study evaluated clinical concordance between PT/INR results to determine the Xprecia Stride analyzer's utility for patient management compared to an FDA-cleared POC device.

Study Purpose

The PT/INR test on the Xprecia Stride Coagulation Analyzer must demonstrate substantial clinical equivalence to an established POC method. Accurate, dependable results facilitate optimal use of the analyzer for assured patient decision making. This study investigated Xprecia Stride analyzer PT/INR result:

- Agreement and bias versus the CoaguChek XS system.
- Clinical concordance versus the CoaguChek XS system.
- Expected range for study subjects not on OAT.
- Repeatability (whole blood).
- Intermediate precision (LQC levels 1 and 2).

Methods

General

Study subjects comprising patients receiving warfarin therapy and individuals not on warfarin therapy were enrolled at four clinical sites* over an 11-month period. Subjects provided two separate fingerstick blood samples. The first finger blood drop was applied within 15 seconds to the CoaguChek XS system, and the second was applied within 15 seconds to the Xprecia Stride analyzer.

Three different lots of Xprecia Stride analyzer test strips were used in a randomized manner at each site. All blood samples were collected and processed according to CLSI H21-A5. Subsequent data analysis was performed by Universal Biosensors Pty Ltd (Rowville, Victoria, Australia).

The study was conducted using reagent test strips, analyzers, and liquid quality control materials manufactured on validated production lines.

Method comparison

Pooled results from the first drop of fingerstick blood from study subjects were used to determine agreement and bias in PT/INR measurement versus the CoaguChek XS system (n = 406). Results were distributed across INRs of 0.9–7.7.

Results were used to perform a Passing-Bablok regression analysis. Slope (95% CI), y-intercept (95% CI), correlation coefficient (r), and coefficient of determination (r^2) were calculated. Passing-Bablok regression acceptance criteria were defined as:

- Slope: 95% confidence interval within 0.80–1.20.
- Intercept: -0.5 to +0.5.
- Coefficient of determination (r^2): ≥0.80.

Bias of the Xprecia Stride method was calculated at two medical decision points (INR = 2.0 and INR = 4.5; see Table 1).

Expected range

Xprecia Stride analyzer PT/INR results (n = 120) from samples provided by individuals not on oral anticoagulant therapy were used to evaluate the expected range. The reference range was reported as the lower and upper INR values encompassing 95% of results.

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Repeatability

The difference between results from pairs of samples taken from two separate fingersticks and tested on the same analyzer was used to assess repeatability. Valid sample pairs from a minimum of 100 study subjects at each clinical site were used for repeatability data analysis. Mean INR, standard deviation, and %CV were calculated for each of four INR ranges (<2.0, 2.0 to 3.0, 3.1 to 4.5, and 4.6 to 8.0; see Table 3).

Intermediate precision

Intermediate precision data were generated by qualified operators at each site performing testing on the Xprecia Stride analyzer with Xprecia System PT Controls (LQC) Level 1 in the normal range, and Level 2 in the therapeutic range, in duplicate for 20 days of testing. Across the four sites, testing was conducted using three lots of reagent test strips and three lots of PT liquid quality control kits. LQC levels 1 and 2 were calculated from complete datasets for each site's analyzer, as shown in Table 4.

Results

Method comparison

Figure 1 shows the all-site Passing-Bablok regression fit for Xprecia Stride analyzer PT/INR results compared to the CoaguChek XS system. Table 1 presents regression statistics and calculated bias.

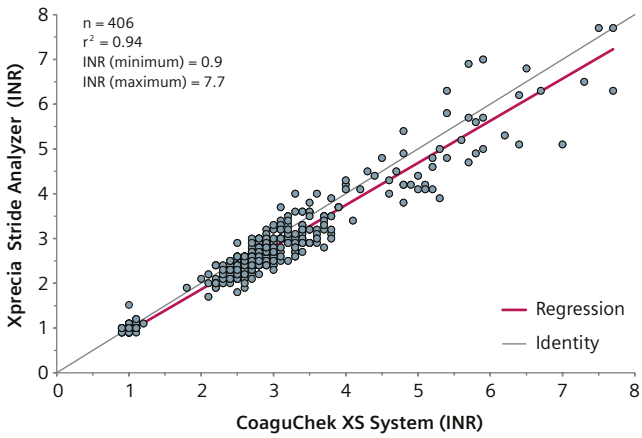

Figure 1. Xprecia Stride analyzer versus CoaguChek XS system PT/INR results: regression fit (red) and line of identity (grey).

Table 1. Xprecia Stride analyzer versus CoaguChek XS system method comparison regression statistics and calculated bias.

Slope (95% CI)	Intercept (95% CI)	Correlation Coefficient (r)	Coefficient of Determination (r^2)	Calculated Bias at 2.0 INR	Calculated Bias at 4.5 INR
0.94 (0.92 to 1.00)	-0.02 (-0.10 to +0.06)	0.97	0.94	-0.14	-0.28

This study demonstrated good correlation of Xprecia Stride analyzer PT/INR results with the CoaguChek XS system method (r^2=0.94).[3] The study also showed the low bias of the test. At the medical decision points of 2.0 INR and 4.5 INR, calculated bias was -0.14 INR and -0.28 INR.

Clinical concordance

Table 2. Xprecia Stride analyzer versus CoaguChek XS system PT/INR result clinical concordance analysis.

	Xprecia Stride Analyzer			
CoaguChek XS System	<2.0 INR	2.0–4.0 INR	>4.0 INR	
<2.0 INR	83 (20.4%)	0 (0%)	0 (0%)	
2.0–4.0 INR	5 (1.2%)	270 (66.5%)	3 (0.8%)	
>4.0 INR	0 (0%)	4 (1.0%)	41 (10.1%)	
				394/406 (97.0%)

Clinical concordance of results was 97.0% using a commonly accepted therapeutic range of 2.0–4.0 INR. Clinical concordance analysis demonstrated high correlation for Xprecia Stride analyzer result classification for the majority of patients (INR below, within, or above reference range; see green shading). Clinical concordance of Xprecia Stride analyzer results over an extended 2.0–4.5 INR therapeutic range (data not shown) was 95.3%.

Expected range

For fingerstick capillary blood on the Xprecia Stride analyzer, an INR range of 0.9 to 1.1 encompassed 95% of results for subjects not on oral anticoagulation therapy.

Repeatability

Table 3. PT/INR results for the Xprecia Stride analyzer on paired samples of fingerstick blood across all four sites.

Xprecia Stride Analyzer Parameter	INR (<2.0)	INR (2.0–3.0)	INR (3.1–4.5)	INR (4.6–8.0)
INR (Mean)	1.0	2.6	3.4	5.5
INR Repeatability (SD)	0.06	0.14	0.19	0.24
INR Repeatability (%CV)	5.8	5.3	5.5	4.4
Sample Pairs	84	220	68	43

Data analysis demonstrated that for all four INR ranges, repeatability CVs were ≤5.8%, well below the industry-standard criterion of acceptance of CV ≤10%.

Overview and Conclusions

Siemens Healthcare's POC Xprecia Stride Coagulation Analyzer was validated according to its intended use with fingerstick blood for clinical PT/INR results across the 0.8–8.0 reportable INR range. The analyzer passed all acceptance criteria in an external study adhering to ICH-GCP guidelines:

- Passing-Bablok regression analysis yielded a slope of 0.94 and an intercept of -0.02, with a coefficient of determination (r^2) of 0.94 across the INR range of 0.9 to 7.7, in a demonstration of performance equivalency with an FDA-cleared alternate POC method (CoaguChek XS system) employing the Dade Innovin reagent.
- Bias against the CoaguChek XS system was low at key medical decision points (-0.14 at 2.0 INR and -0.28 at 4.5 INR).
- Clinical concordance of Xprecia Stride analyzer PT/INR results versus the CoaguChek XS system was 97.0% using a commonly accepted therapeutic range of 2.0–4.0 INR.
- Repeatability demonstrated CVs ≤5.8% across the reportable range, well below the criterion of acceptance of ≤10% CV.[3]
- Intermediate precision was ≤7.0% CV, also meeting the ≤10% CV acceptance criterion.

The Xprecia Stride analyzer has equivalent performance to an FDA-cleared PT/INR POC test. Trained healthcare professionals can confidently use the Xprecia Stride test at the point of care to monitor patients on warfarin oral anticoagulant therapy.

The reliable, lab-like performance of the Xprecia Stride analyzer is complemented by its speed, simplicity, efficiency, and overall practicality in POC settings.

References

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Intermediate Precision

Table 4. Intermediate precision of LQC testing for each study location.

Analyzer	Parameter	LQC Level 1	LQC Level 2
Site 1	Data Pairs	40	40
	Mean INR	1.27 (Target 1.2)	3.18 (Target 2.9)
	Repeatability (SD)	0.03	0.06
	Repeatability (%CV)	2.5	1.8
	Within-laboratory SD	0.05	0.15
	Within-laboratory %CV	3.9	4.9
Site 2	Data Pairs	40	40
	Mean INR	1.29 (Target 1.2)	3.22 (Target 3.1)
	Repeatability (SD)	0.03	0.07
	Repeatability (%CV)	2.3	2.2
	Within-laboratory SD	0.04	0.10
	Within-laboratory %CV	2.8	3.1
Site 3	Data Pairs	40	40
	Mean INR	1.20 (Target 1.2)	3.18 (Target 3.2)
	Repeatability (SD)	0.02	0.05
	Repeatability (%CV)	1.9	1.6
	Within-laboratory SD	0.02	0.08
	Within-laboratory %CV	1.9	2.7
Site 4	Data Pairs	40	40
	Mean INR	1.24 (Target 1.2)	3.11 (Target 2.9)
	Repeatability (SD)	0.04	0.11
	Repeatability (%CV)	3.3	3.6
	Within-laboratory SD	0.06	0.22
	Within-laboratory %CV	4.6	7.0

Data analysis demonstrated that for all four sites, intermediate precision CVs were ≤7.0%, well below the industry-standard criterion of acceptance of CV ≤10%.

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