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White Paper

PT/INR Test Performance of the Xprecia Stride Coagulation Analyzer on Capillary Blood is Equivalent to a Reference Laboratory Hemostasis System

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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 oral anticoagulant therapy (OAT).

The Xprecia Stride™ Coagulation Analyzer* from Siemens Healthcare Diagnostics is a novel, handheld POC device that generates rapid PT/INR test results from fingerstick samples. This external validation study, conducted under ICH/GCP** guidelines, assessed the clinical substantial equivalence of the Xprecia Stride analyzer PT/INR test against an established laboratory hemostasis method (BCS® XP System, Siemens Healthcare Diagnostics).

Summary

Method comparison between the Xprecia Stride analyzer and the BCS XP System demonstrated excellent correlation (R^2=0.91) and a low bias ranging from -0.13 INR to 0.01 INR at medical decision levels.

Intermediate precision demonstrated that Liquid Quality Control (LQC) met the industry-standard acceptance criterion of ≤ 10%. In addition, repeatability using patient samples was also found to be well within the same acceptance criterion.

The data and subsequent analysis validate the intended clinical use of the Xprecia Stride Coagulation Analyzer for near-patient PT/INR testing using capillary blood.

*Not available for sale in the U.S. Product availability varies by country.
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PT/INR Test Performance of the Xprecia Stride Coagulation Analyzer on Capillary Blood

The Increasing Demand for Oral Anticoagulant Therapy

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 (AF), a common cardiac arrhythmia that affects more than six 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 the medications usually necessitate frequent patient INR monitoring.

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 away from the central laboratory have escalated the demand for PT/INR tests at the point of care:

- POC PT/INR test settings include the physician's office, outpatient clinics, and diverse hospital locations, including the emergency room, coronary care unit, operating rooms, and the radiography department
- PT/INR testing at the point of care facilitates rapid interventions that may help to optimize patient therapy

Clinical Utility

The Xprecia Stride Coagulation Analyzer is intended for near-patient monitoring of PT/INR testing on capillary blood samples. It is an accurate, convenient, easy-to-use handheld instrument with enhanced safety features designed to protect operators during the testing process:

- Fast results across the 0.8–8.0 PT/INR reporting range
- Small, 6 µL sample size
- Push-button ejection of used test strips to minimize biohazard exposure
- Easy-to-use color touchscreen interface and clear display of results as PT/INR units or PT seconds
- Integrated barcode scanner to facilitate rapid, error-free data capture
- Seamless, secure bi-directional data transfer via USB connection

Test Technology

The Xprecia Stride analyzer uses 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 by capillary action.

The strip contains dried reagents consisting of thromboplastin, an electro-active thrombin substrate, and other reagents. An electro-active group, released from the thrombin substrate, is detected electrochemically at the electrodes in the strip; the current produced is analyzed by an algorithm to determine the coagulation time. Each test strip is analyzed by two on-strip quality control checks when a sample is applied: to check for presence of adequate test sample and reagents on the test strip, and to check for test strip degradation due to exposure to environmental factors. If either control fails, the analyzer will report an error and cancel the test.

Liquid Quality Control (LQC) material offers users the option of testing in accordance with local, state, federal, or national guidelines.

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

The Xprecia Stride analyzer uses the Dade® Innovin® reagent—the same reagent used by Siemens' lab analyzers—removing a potential area for variability between lab and POC test results.

Study Purpose

The PT/INR test on the Xprecia Stride Coagulation Analyzer must demonstrate clinical substantial equivalence to the clinical reference method. Accurate results—in terms of precision and low bias—facilitate optimal use of the analyzer for clinical decision-making. The study investigated:

- Agreement versus a proven reference laboratory method used for PT/INR testing
- Intermediate precision (LQC levels 1 and 2)
- Repeatability
- Expected PT/INR range for study subjects not on anticoagulation therapy

Methods

General

One hundred study subjects, comprising patients receiving warfarin therapy and individuals not on warfarin therapy, were enrolled at four clinical sites* over a seven-week period. At each site, subjects provided two separate whole blood capillary samples via finger puncture for immediate PT/INR testing by qualified POC operators on the Xprecia Stride Coagulation Analyzer. Each subject also provided a whole blood sample collected in a citrated tube. These samples were centrifuged to generate platelet-poor plasma and then frozen. Frozen samples were shipped to a laboratory** for PT/INR testing on the reference Siemens BCS XP System using Dade Innovin reagent. The same aliquot of sample was measured twice, and the PT/INR results averaged to give the laboratory PT/INR value. Subsequent data analysis was performed by Universal Biosensors Pty Ltd (Rowville, Victoria, Australia).

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

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Method Comparison Study

Results from the first drop of fingerstick whole blood from study subjects (N=99) were used to determine agreement and bias in PT/INR measurement. Xprecia Stride analyzer results across four PT/INR ranges (< 2.0, 2.0 to 4.5, 4.6 to 6.0, and 6.1 to 8.0) were used for method comparison. These ranges provided a distribution of subject results across the measuring range. Study subjects were allocated to a range based on their averaged laboratory PT/INR reference value.

Results from both analytical methods were used to perform a weighted Deming regression. The slope (95% CI), y-intercept (95% CI), correlation coefficient (R), and coefficient of determination (R^2) were calculated. Deming regression acceptance criteria up to 6.0 INR were defined as:

- Slope: 95% confidence interval within 0.80–1.20
- Intercept: +0.3 to -0.3
- Coefficient of determination (R^2) ≥ 0.82

Bias for the Xprecia Stride analyzer PT/INR test was calculated at two medical decision points (PT/INR=2.0 and PT/INR=4.5, see Table 1).

Intermediate Precision Study

Intermediate precision data was generated by qualified operators at each site performing tests on the Xprecia Stride analyzer with LQC levels 1 and 2 in duplicate during 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. The multiple parameters calculated from complete datasets for each site analyzer at each LQC level are shown in Table 3.

Repeatability Study

Difference between results from pairs of capillary samples taken from two separate finger-sticks and tested on the same analyzer was used to assess repeatability. Valid pairs from 100 study subjects (all clinical sites) were used for repeatability data analysis. Mean PT/INR, the standard deviation, and the %CV were calculated across four PT/INR ranges (< 2.0, 2.0 to 3.0, 3.1 to 4.5, and 4.6 to 8.0, see Table 2).

Expected Range

Xprecia Stride analyzer PT/INR test results (N=120, 84 results sourced from this study, combined with 36 results from an in-house study) were used to evaluate the expected range for non-therapeutic individuals. The normal range was reported as lower and upper INR values enclosing 95% of results.

Results

Method Comparison Study

Figure 1 shows a plot of the weighted Deming regression performed on capillary blood PT/INR results from Xprecia Stride analyzers compared to PT/INR results with the reference BCS XP System. Table 1 presents method comparison regression statistics and calculated bias.

Figure 1. Plot of weighted Deming regression fit (red) and line of identity (grey).

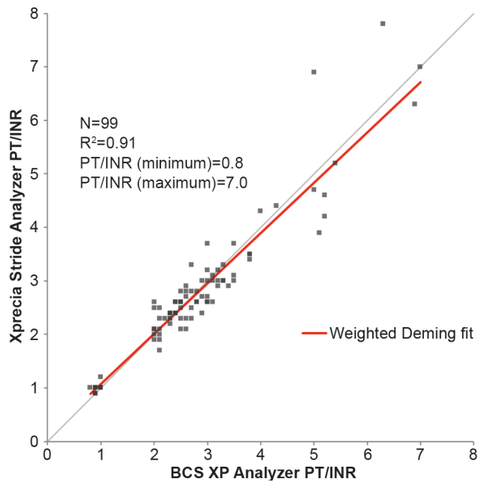

Table 1. Xprecia Stride analyzer versus BCS XP System method comparison regression statistics, and calculated bias.

Slope (95% CI)	Intercept (95% CI)	Correlation Coefficient (R)	Coefficient of Determination (R^2)	Calculated Bias at 2.0 PT/INR	Calculated Bias at 4.5 PT/INR
0.946 (0.901 to 0.991)	0.12 (0.05 to 0.18)	0.956	0.91	0.01	-0.13

This study demonstrated excellent correlation (R^2=0.91) of the Xprecia Stride Coagulation Analyzer PT/INR test with the reference laboratory BCS XP System method.[3]

The study also showed the low bias of the test compared with laboratory BCS XP System PT/INR measurement. At the medical decision points of 2.0 PT/INR and 4.5 PT/INR, bias was ≤ ± 0.13 PT/INR, well within the acceptance criterion defined as not to exceed a median bias of ± 0.3.

Repeatability Study

Table 2. PT/INR results for the Xprecia Stride analyzer on paired samples of capillary blood.

	Validated PT/INR (< 2.0)	Validated PT/INR (2.0 –3.0)	Validated PT/INR (3.1–4.5)	Validated PT/INR (4.6–8.0)
PT/INR (Mean)	1.00	2.52	3.31	5.68
Repeatability (SD)	0.06	0.10	0.14	0.20
Repeatability (%CV)	5.9	4.1	4.2	3.6
PT/INR (Minimum)	0.9	1.7	2.8	3.9
PT/INR (Maximum)	1.1	3.65	4.4	7.7
Sample Pairs (Number)	20	53	18	9
Total Results (Number)	40	106	36	18

Data analysis demonstrated that across the four PT/INR ranges, repeatability %CVs were ≤ 5.9, well below the industry-standard criterion of acceptance of %CV ≤ 10%.

Expected Range

For capillary blood, the Xprecia Stride analyzer PT/INR test range 0.9 to 1.1 enclosed 95% of results for subjects not on oral anticoagulation therapy.

Intermediate Precision Study

Table 3. Intermediate precision of PT Liquid Quality Control (LQC) testing across study locations.

	Parameter	LQC Level 1	LQC Level 2
Site 1	Data Pairs	40	40
	Mean PT/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 PT/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 PT/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 PT/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

Discussion and Conclusions

The Xprecia Stride Coagulation Analyzer was validated according to its intended use with capillary blood. All test acceptance criteria over the measuring range were passed, with the following Deming regression results:

- Slope: 0.946 (95% CI 0.901 to 0.991)
- Intercept: 0.12 (95% CI 0.05 to 0.18)
- Coefficient of determination (R^2) ≥ 0.91

The PT/INR test showed equivalency when compared to the PT/INR test of the reference BCS XP System. Bias was notably low at two key PT/INR medical decision points (2.0 PT/INR, bias 0.01, and 4.5 PT/INR, bias -0.13). Intermediate precision was ≤ 7.0 %CV, meeting an acceptance criterion of ≤ 10 %CV. Test repeatability was ≤ 5.9 %CV, also well below this criterion of acceptance.[3]

The Xprecia Stride analyzer PT/INR test has equivalent performance to a reference lab test. Trained healthcare practitioners can confidently use the test at the point of care to monitor patients on warfarin oral anticoagulant therapy.

The reliable, lab-quality performance of the Xprecia Stride Coagulation Analyzer is complemented by its speed, simplicity, efficiency, and overall practicality in point-of-care settings.

PT/INR Test Performance of the Xprecia Stride Coagulation Analyzer on Capillary Blood

References

1. Kannel WB, and Benjamin EJ. Status of the epidemiology of atrial fibrillation. Med. Clin. North Am., 2008;92:17-40.
2. Jackson CM, and Esnouf MP. Clin. Chem., 2005;51(3):483-485.
3. Clinical laboratory testing and in vitro medical devices – Requirements for in vitro monitoring systems for self-testing of oral anticoagulant therapy. ISO 17593:2007.