A Validation Study for the Quantitative Measurement of the Prothrombin Time/International Normalized Ratio (PT/INR) Test on the Xprecia Stride Coagulation Analyzer* for Warfarin Monitoring

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Abstract

Objective: The Xprecia Stride™ Coagulation Analyzer from Siemens Healthcare Diagnostics (SHD) is a novel, handheld POC device that generates rapid PT/INR results from fingerstick samples for oral anticoagulant therapy monitoring (OAT). This external validation study, conducted under the International Conference on HarmonizationGood Clinical Practice (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).

Methods: Test methods were based on the following Clinical Laboratory Standards Institute (CLSI) guidelines: 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-A3).

Results: Weighted Deming regression analysis yielded a slope of 0.95 and an intercept of -0.12, with R² = 0.91 across the range of 0.8 to 7.0 INR. Repeatability using whole blood demonstrated NCVs were <5.9 across the reportable range. LQC at two levels demonstrated repeatability precision NCVs that were <6% and within laboratory NCVs that were <7.0. The Expected Range for the PT/INR on the Xprecia Stride analyzer was 0.9 to 1.1 for subjects not on OAT.

Conclusion: The Xprecia Stride analyzer PTINR test results were substantially equivalent to those of the BCS XP System.

Background

The Xprecia Stride analyzer is intended for multiple-patient use by professional healthcare providers for quantitative prothrombin time testing for the monitoring of oral anticoagulation therapy with warfarin, a vitamin K antagonist. The system uses fresh capillary whole blood and is intended for professional in vitro diagnostic use at the point of care.

A clinical trial was conducted with subjects currently on warfarin therapy and subjects not receiving warfarin therapy. The study took place at four sites with a minimum of three typical point-of-care operators. The study was performed:

- Demonstrate clinical substantial equivalence of capillary samples with the laboratory method, using Dade® Innovin® recombinant human tissue thromboplastin reagent (INR vs. INR).
- Demonstrate clinical substantial equivalence of capillary samples with the Roche Coaguchek® X5 analyzer (INR vs. INR).
- Validate the repeatability of the Xprecia Stride PTINR analyzer across the measuring range of capillary samples.
- Validate the hematocrit range of the Xprecia Stride analyzer.
- Demonstrate intermediate precision using two levels of PT liquid quality controls (LQC) at each site analyzed in duplicate, every day for a minimum of 20 days.

Methods

Recruitment of subjects

- Subjects who participated in this study were enrolled from clinics for routine PTINR monitoring.
- Participation was voluntary and consented.

Blood sampling, handling of specimens and measurements

- All samples for testing on the Xprecia Stride analyzer were capillary samples.
- Two separate fingerstick samples were taken using the first drop of the first fingerstick for the CoaguChek XS analyzer results and the first drop of the second fingerstick for the Xprecia Stride analyzer results.

Xprecia Stride analyzer results

- Each sample was tested on one Xprecia Stride PTINR analyzer and one CoaguChek XS analyzer.
- Three different lots of Xprecia Stride analyzer test strips were used at each site during the course of the study.
- One lot of CoaguChek XS analyzer test strips was used.
- Samples for the central laboratory device were obtained from a venous puncture and collected into one tube with 0.2% (0.199 M) sodium citrate. The tube was mixed thoroughly and centrifuged to obtain platelet-poor plasma. The plasma was shipped frozen to a laboratory site to be tested on a BCS XP laboratory analyzer using Dade Innovin reagent in duplicate.
- One tube with EDTA was collected to be tested on the site’s laboratory instrument for hematocrit.

Xprecia Stride analyzer methodology

- The device uses electrochemical technology to measure the PTINR. A sample chamber in the strip is filled with blood sample by capillary action. The strip contains dried reagents consisting of the Dade Innovin thromboplastin, an electroactive thrombin substrate, and other reagents. An electroactive group, released from the thrombin substrate, is detected at the electrodes in the strip; the current produced is analyzed by an algorithm to determine the result.

Table 1. Repeatability: capillary blood

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<th>Parameter</th>
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<th>LQC 2</th>
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<td>Within-laboratory INR</td>
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<td>Within-laboratory NCV</td>
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<td>Repeatability NCV</td>
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<td>Within-laboratory NCV</td>
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<td>Within-laboratory NCV</td>
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Table 2. Intermediate precision: liquid quality control

<table>
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<tr>
<th>Parameter</th>
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</tr>
</tbody>
</table>

Figure 1. Method comparison: Xprecia Stride analyzer vs. BCS XP system.

Figure 2. Factor sensitivity.

Figure 3. Hematocrit.

Figure 4. Method comparison: Xprecia Stride analyzer vs. BCS XP system.

Figure 5. Percent difference of Xprecia Stride analyzer INR to BCS XP INR plotted against the mean of the BCS XP INR.

Figure 6. Method comparison Xprecia Stride analyzer vs. CoaguChek analyzer.

Figure 7. Percent difference of Xprecia Stride analyzer to CoaguChek XS analyzer INR plotted against the mean of the CoaguChek XS INR and the Xprecia Stride analyzer INR.

Conclusions

- The Xprecia Stride analyzer is validated according to its intended use with capillary blood samples for a range of 0.8 to 8.0 INR.
- The repeatability precision using whole blood meets the system acceptance criteria for all INR ranges.
- The intermediate precision using levels 1 and 2 of the PT liquid quality controls meets the system precision acceptance criteria.
- Typical Xprecia Stride analyzer PTINR test sensitivity to factors II, V, VII, and X was evaluated to characterize the effects of the intrinsic coagulation factors, and the results are represented graphically above.
- It has been verified that over the hematocrit range of 20 to 48% there is no significant effect of sample hematocrit on the INR result.
- The expected INR range for healthy subjects not on anticoagulant therapy is 0.9 to 1.1 for capillary blood samples.

References


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

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