Multicenter evaluation of the CoaguChek® Prothrombin Time (PT) Test on the CoaguChek® Pro II meter

White paper

CoaguChek® Pro II
The Bold Standard.

CoaguChek®
Because it's my life

Contents

Summary 3

Introduction 4

Intended use 4

Fields of application 4

Enhanced features of the CoaguChek Pro II system compared with other CoaguChek systems 5

Study data 6

Method comparison with reference methods 6

Fig. 1. Passing–Bablok regression analysis of INR values for the CoaguChek Pro II system compared with the Siemens Dade Innovin PT test 6

Sensitivity in patients with documented coagulation deficiencies 7

Repeatability study 7

Table 1. Repeatability of INR values and PT values in seconds measured with the CoaguChek PT Test strip on the CoaguChek Pro II meter 7

Intermediate precision and reproducibility study 7

Table 2. Intermediate precision and reproducibility of INR values determined with the CoaguChek PT Test strip on the CoaguChek Pro II meter across four study sites combined 7

Sample matrix comparison study 8

Table 3. Sample matrix comparison for capillary and arterial blood versus venous blood using the CoaguChek aPTT Test strip on the CoaguChek Pro II meter 8

Interfering substances 8

User performance evaluation 8

Conclusions 8

CoaguChek Pro II meter and CoaguChek PT Test strip specifications 9

References 10

Summary

Rapid and reliable determination of the prothrombin time (PT) and international normalized ratio (INR) is vital in a wide range of clinical scenarios. The CoaguChek Pro II is the latest addition to the CoaguChek point-of-care (POC) coagulation systems from Roche. The CoaguChek Pro II system uses the new CoaguChek PT Test strip which has a broader intended use compared with the predecessor CoaguChek XS PT Test strip. This external validation study evaluated the analytical performance of the CoaguChek PT Test on the CoaguChek Pro II meter and compared this performance with an approved laboratory method.

All study endpoints were successfully met. INR values measured on the CoaguChek Pro II system demonstrated excellent correlation to those measured on the Sysmex® CA-1500 laboratory reference analyzer using the Siemens® Dade® Innovin® PT reagent (Pearson's r = 0.98) with very low bias (relative mean difference 0.2%). The CoaguChek Pro II system delivered INR values and PT values in seconds with high precision. The pooled coefficient of variation (CV) in the repeatability studies with venous patient samples was 3.3% for INR and 2.3% for PT in seconds. Intermediate precision using CoaguChek PT controls was excellent (< 3.0% CV).

Test results were comparable when measured in either venous or capillary blood. Similar results were seen with arterial samples, though only a few of these samples were available for analysis. There was no evidence of systematic interference on the CoaguChek PT Test strip with any of the potential interferents analyzed.

These data confirm that the CoaguChek Pro II system delivers reproducible and laboratory-comparable PT/INR test results and validate its use at the Point of Care.

Introduction

Clinical situations often demand fast and accurate assessment of a patient's coagulation status. This is particularly important in emergency and acute care settings. An increasing number of patients worldwide with conditions including atrial fibrillation, deep vein thrombosis, and pulmonary embolism are treated with oral anticoagulation therapies such as Vitamin K antagonists (VKA) to reduce the risk of abnormal blood clots developing.[1] There are also groups of patients who present with hereditary or acquired deficiencies in coagulation factors of the extrinsic and common pathways. Many of these individuals have an elevated risk of bleeding compared with those with normal coagulation function. Tests such as the PT/INR and the activated partial thromboplastin time (aPTT) are established methods for investigating coagulopathies and contribute vital information to clinical decision-making based on an individual's coagulation status.[2] In acute care settings such as the emergency department (ED), intensive care unit (ICU), or operating room (OR), POC coagulation testing provides test results in real time and enables multidisciplinary care teams to make immediate, informed treatment decisions.

The PT test is a global assay of the extrinsic and common coagulation pathways.[3] It is commonly used to detect inherited and acquired coagulation disorders, to assess liver function, to evaluate hemostasis in bleeding patients and prior to invasive procedures in selected patients, and to monitor VKA therapy.[2,4–7]

For over 20 years CoaguChek systems from Roche have set the standard in POC coagulation monitoring, delivering fast and accurate PT/INR test results — whether through patient self-testing or testing by healthcare professionals at the Point of Care. The CoaguChek Pro II system from Roche is optimized for use within acute care settings and now offers both the PT/INR and aPTT tests on a single POC system. Each CoaguChek PT Test strip lot is pre-calibrated against the World Health Organization (WHO) reference method ensuring accuracy of the test results. The PT/INR values are provided within approximately one minute.

Intended use

The CoaguChek Pro II system (comprised of the CoaguChek Pro II meter, the CoaguChek PT Test and CoaguChek aPTT Test strips) is used for the determination of PT and aPTT by healthcare professionals in a point-of-care environment.

The CoaguChek PT Test is an *in vitro* assay for the determination of PT using the CoaguChek Pro II meter. The test can be used with either capillary, venous, or arterial fresh whole blood.

Fields of application

The CoaguChek PT Test is a one-step coagulation test using human recombinant tissue factor as an activator.

The CoaguChek PT Test can be used:

- for the determination of the PT in patients with suspected deficiencies of coagulation factors of the extrinsic and common pathway, with the exception of fibrinogen
- for monitoring of patients on oral anticoagulant therapy with VKAs

Enhanced features of the CoaguChek® Pro II system compared with other CoaguChek® systems

The CoaguChek Pro II system offers multiple enhancements over the CoaguChek XS Plus and CoaguChek XS Pro systems, including a broader operating temperature range and an extended test menu.

The CoaguChek XS PT Test was optimized to be insensitive to levels of unfractionated and low molecular weight heparin (LMWH) up to 3 IU/mL, and is now called the CoaguChek PT Test. The CoaguChek PT Test has a wider intended use compared with the CoaguChek XS PT Test: the CoaguChek Pro II system can be used to determine PT in patients with suspected deficiencies of coagulation factors of the extrinsic and common pathways, with the exception of fibrinogen. The system also supports VKA therapy monitoring in hospital and outpatient settings including anticoagulation clinics and physicians' offices. Both the CoaguChek PT and aPTT Test strips deliver accurate results across a broad hematocrit range (15 – 55%) ensuring fast and reliable assessment of coagulation status in individuals with low hematocrit values, such as anemic patients and those in the ICU.

The CoaguChek Pro II system has enhanced connectivity compared with other CoaguChek systems for professional use. Built-in Wi-Fi connectivity allows test results to be immediately transmitted from the meter to the dedicated data management system or a patient's electronic health record via the wireless local area network (WLAN) and compatible middleware. Hence vital information is available in real time at every Point of Care, eliminating transcription steps, thereby reducing the possibility of human error, and streamlining workflow.

Using the first-in-market QR code feature for POC coagulation systems, a test result on the CoaguChek Pro II meter can be converted into a QR code which is compatible with the relevant data management system's requirements, be it plain text, coded data or data transmitted via a URL. This QR code can then be scanned using either a barcode reader or any smart device (e.g. a tablet or a smart phone) scan app, and transmitted to the data management system, making test results immediately accessible to healthcare professionals who can then make appropriate treatment decisions in real time.

Study data

The performance of the CoaguChek PT Test on the CoaguChek Pro II meter was verified in a study performed at four external clinical sites.† Testing was conducted using fresh whole blood samples from patients representative of the European adult population with an indication for the assessment of coagulation status who were recruited from different clinical settings (the ED, ICU, hematology center, and OR).

Method comparison with reference methods

The CoaguChek PT Test on the CoaguChek Pro II meter demonstrated excellent correlation with the Siemens Dade Innovin PT laboratory reference test (Pearson's r = 0.98 for both INR [Figure 1] and PT in seconds). All CoaguChek INR values, and 98% of CoaguChek PT values in seconds, were within ± 25% of Innovin INR/PT values across the tested INR range. The relative mean difference of INR values between tests was 0.2%. The relative mean difference for PT values in seconds was higher (10.1%) as expected due to the lack of standardization of this unit.

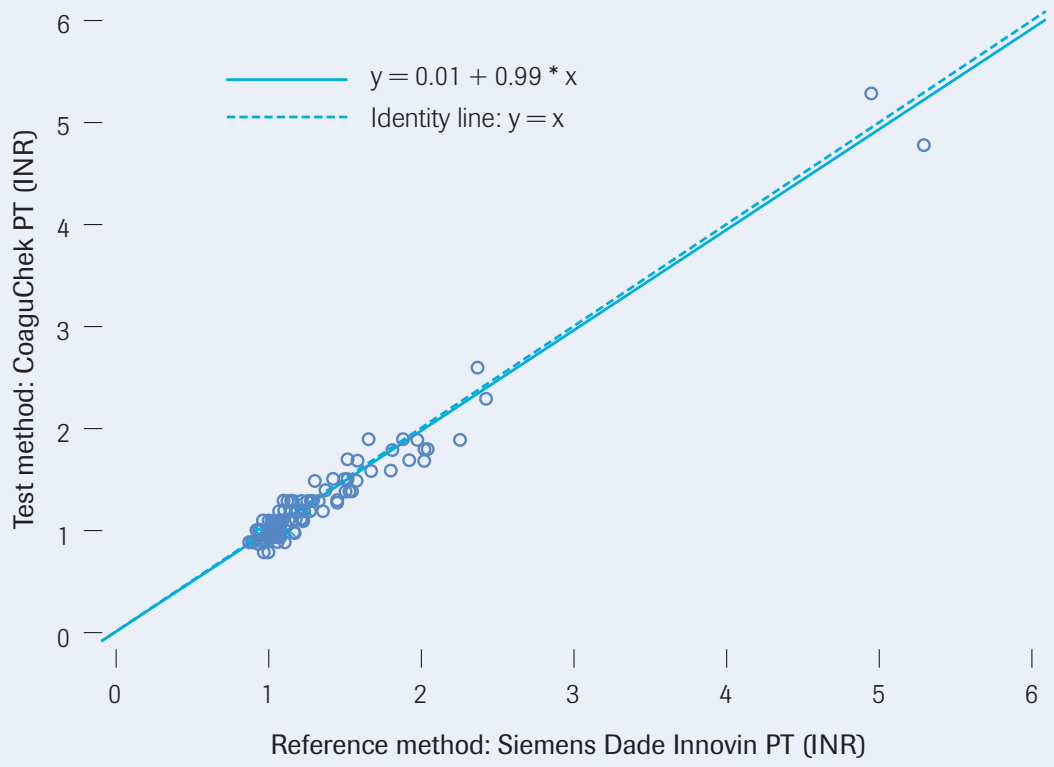

Fig.1. Passing–Bablok regression analysis of INR values for the CoaguChek Pro II system compared with the Siemens Dade Innovin PT test (all sites combined excluding outliers; n = 256; slope 0.99; intercept 0.01; Pearson's r = 0.98)

†1. Med. Versorgungszentrum IMD GmbH, Gerinnungspraxis Mannheim, Mannheim, Germany (Principal Investigator [PI] Prof. Dr. Carl-Erik Dempfle); 2. Universitätsklinikum Heidelberg, Medizinische Klinik IV, Gastroenterologie, Heidelberg, Germany (PI Dr. Anita Pathil-Warth); 3. Vienna Hospital Association, Allgemeines Krankenhaus-Universitätskliniken, Notfallmedizin, Vienna, Austria (PI Univ. Prof. Dr. Anton Laggner); 4. Krankenhaus St. Vinzenz Zams, Innere Medizin, Zams, Austria (PI Dr. Hans Robert Schönherr).

Sensitivity in patients with documented coagulation deficiencies

Twenty-four patients from site 1 had documented coagulation factor deficiencies. The PT values measured in these patients' samples on the CoaguChek Pro II system demonstrated very good concordance with the laboratory reference test. All results were equivalent when both the 97.5th percentile of a reference population and 1.5-fold the mean normal value were used as cut-offs to define positive and negative results with the two tests. These data demonstrate that the CoaguChek PT Test on the CoaguChek Pro II meter has a comparable sensitivity to the Siemens Dade Innovin PT test for detecting patients with coagulation factor deficiencies.

Repeatability study

The distribution of INR values reflected the clinical settings from which the patients were recruited, with most showing low INR values (Table 1). For all patients combined the pooled CV for INR values was 3.3% and 2.3% for PT in seconds. The pooled CVs for INR values and PT values in seconds across the different INR ranges were also low (< 3.6% and < 2.4%, respectively).

		CoaguChek® PT (INR)		CoaguChek® PT (sec)	
	n[a]	Mean	%CV_{pool} (95% CI)	Mean	%CV_{pool} (95% CI)
All sites combined	68	1.54	3.3 (2.8, 4.0)	18.5	2.3 (2.0, 2.8)
INR ≤ 1.2[b]	42	1.05	3.6 (3.0, 4.6)	12.6	2.4 (2.0, 3.0)
INR 1.3 – 1.9[b]	19	1.63	3.0 (2.3, 4.4)	19.6	2.4 (1.8, 3.5)
INR ≥ 2.0[b]	7	4.22	2.0 (1.3, 4.3)	50.7	1.9 (1.2, 4.2)

Repeatability was analyzed in two runs on six CoaguChek Pro II systems resulting in 12 replicates per sample; [a] n is the number of series (68 in total from 55 patients; some patients were tested twice on different test strip lots); [b] INR range was determined using the CoaguChek Pro II system. CI, confidence interval.

Table 1. Repeatability of INR values and PT values in seconds measured with the CoaguChek PT Test strip on the CoaguChek Pro II meter

Intermediate precision and reproducibility study

Intermediate precision and reproducibility with CoaguChek PT controls was excellent with low CVs for both the Level 1 and Level 2 controls (Table 2).

			Intermediate precision		Reproducibility	
CoaguChek® control level	n	Mean INR	SD	%CV (UCI)	SD	%CV (UCI)
Level 1	336	1.3	0.0	3.0 (3.2)	0.0	3.2 (3.6)
Level 2	336	3.0	0.1	2.3 (2.4)	0.1	3.1 (4.1)

Intermediate precision and reproducibility was determined using CoaguChek PT Level 1 and Level 2 controls according to guidelines from the Clinical and Laboratory Standards Institute (CLSI EP5-A2).[8] Controls were measured over 21 days in two runs per day using two or three lots of CoaguChek PT Test strips. Data from all four sites were combined. SD, standard deviation; UCI, upper confidence interval (one-sided 95% CI).

Table 2. Intermediate precision and reproducibility of INR values determined with the CoaguChek PT Test strip on the CoaguChek Pro II meter across four study sites combined

Sample matrix comparison study

There was no difference in INR values and PT values in seconds when measured with the CoaguChek Pro II system in either venous or capillary whole blood samples. The relative mean difference for both coagulation units was low (< 0.5%), indicating that either sample type can be used with the CoaguChek Pro II system. Similar results were seen for arterial samples compared with venous samples; however, only a low number of these samples were available for analysis.

	CoaguChek® PT (sec)		CoaguChek® PT (INR)
Comparison	n[a]	RMD[b] (95% CI)	RMD[b] (95% CI)
Capillary vs. venous	66	0.2 (–1.0, 1.5)	0.4 (–0.5, 1.4)
Arterial vs. venous	13	0.4 (–2.6, 3.5)	0.4 (–1.0, 1.7)

[a] n is the number of patients; [b] RMD, relative mean difference in percent.

Table 3. Sample matrix comparison for capillary and arterial blood versus venous blood using the CoaguChek PT Test strip on the CoaguChek Pro II meter

Interfering substances

Levels of electrolytes (sodium, chloride), bilirubin, triglycerides, fibrinogen, platelets, and hematocrit were determined in patient samples and plotted against the deviation of PT in seconds measured on the CoaguChek Pro II system versus the Siemens Dade Innovin PT test. None of the tested interferents significantly impacted on the CoaguChek PT Test results. In all cases the bias difference between the CoaguChek PT Test and the Siemens Dade Innovin reference test at the highest and the lowest interference concentration was below 22%. INR values measured on the CoaguChek Pro II system were unaffected by hematocrit values in the tested hematocrit range of 18.9 to 51.4%.

User performance evaluation

Operators participating in this study completed a questionnaire to evaluate the usability of the CoaguChek Pro II system. Overall, the operators rated the ease of handling of the CoaguChek Pro II meter as good, with the majority of users agreeing that performing a test on the system was easy.

Conclusions

All endpoints were successfully met in this study, validating the analytical performance of the CoaguChek PT Test on the CoaguChek Pro II meter. The CoaguChek Pro II system provides INR values and PT in seconds with very high reproducibility and generates results that are comparable to the Siemens Dade Innovin PT test used as the reference laboratory method. PT/INR test results provided by the CoaguChek Pro II system are unaffected by the sample type used.

In a limited population of patients with documented coagulation factor deficiencies, the CoaguChek PT Test strip had comparable sensitivity to that of the Siemens Dade Innovin PT laboratory reference test.

The CoaguChek Pro II meter with the CoaguChek PT Test strip can be used by healthcare professionals to obtain immediately actionable coagulation results at all Points of Care. Whether this is to determine if a patient has a coagulation factor deficiency of the extrinsic or common pathways or for monitoring VKA therapy, the CoaguChek Pro II system delivers reliable information when and where it is needed the most.

CoaguChek® Pro II meter and CoaguChek® PT Test strip specifications

Measuring and sampling	
Detection system	Amperometric (electrochemical) determination after activation of the blood coagulation with human recombinant thromboplastin
User interface	Full graphical (thin-film-transistor)
Support and safety functions	QC lockout, patient & user ID, protection with administrator ID, 2D barcode scanner
Sample application	Outside the meter, with top- and two sides (left or right)-dosing options
Operating conditions	
Operating temperature	+12 to +32°
Operating humidity and altitude	10 – 85%; 4,300 m (14,000 ft)
Handling	Operating the meter: on a level, vibration free surface, in a roughly horizontal position
Measuring range	PT/INR: 0.8 – 8.0; %Quick: 120 – 5; seconds: 9.6 – 96
Memory	2,000 patient and 500 QC results with date and time 120 code chip records (60 strip codes & 60 control codes) Operator list with up to 5,000 operator IDs with corresponding 2nd ID e.g. operator name Patient list with up to 4,000 patient IDs with corresponding 2nd and 3rd patient IDs e.g. name, date of birth
Interface	Touch screen and barcode scanner
Power options	Universal battery pack for the CoaguChek Pro II meter Power supply adapter: input: 100 – 240 V / 50 – 60Hz / 350 – 150 mA; output: 12 V DC / 1.25 A
Number of tests with fully charged battery pack	Approximately 60 tests
Dimensions	187 x 97 x 43 mm
Weight (without batteries)	280 g
Safety class	III
Auto power off	Programmable, 1 to 60 minutes
Sample material	
Sample type	Capillary, venous, or arterial fresh whole blood
Sample size	≥ 8 µL
Interferences	As listed in the CoaguChek PT Test method sheet
Test strips	
ISI	Approximately 1.0
Sensitivity to heparin	Insensitive to unfractionated and fractionated heparin concentrations up to 3 IU/mL
Quality control	On each test strip, through the same channel as the blood passes
Stability	Storage at +2 to +30°C. Test strips can be used until expiry date printed on the box and test strip vial

References

1. *Nutescu, E.A., Wittkowsky, A.K., Burnett, A., Merli, G.J., Ansell, J.E., Garcia, D.A. (2013). Delivery of optimized inpatient anticoagulation therapy: consensus statement from the Anticoagulation Forum.* Ann Pharmacother *47, 714–724.*

2. *Haas, T., Fries, D., Tanaka, K.A., Asmis, L., Curry, N.S., Schöchl, H. (2015). Usefulness of standard plasma coagulation tests in the management of perioperative coagulopathic bleeding: is there any evidence?* Br J Anaesth *114, 217–224.*

3. *Tripodi, A., Lippi, G., Plebani, M. (2016). How to report results of prothrombin and activated partial thromboplastin times.* Clin Chem Lab Med *54, 215–222.*

4. *Tripodi, A., Caldwell, S.H., Hoffman, M., Trotter, J.F., Sanyal, A.J. (2007). Review article: the prothrombin time test as a measure of bleeding risk and prognosis in liver disease.* Aliment Pharmacol Ther *26, 141–148.*

5. *Spahn, D.R., Bouillon, B., Cerny, V., Coats, T.J., Duranteau, J., Fernández-Mondéjar, E. et al. (2013). Management of bleeding and coagulopathy following major trauma: an updated European guideline.* Crit Care Lond Engl *17, R76.*

6. *Chee, Y.L., Crawford, J.C., Watson, H.G., Greaves, M. (2008). Guidelines on the assessment of bleeding risk prior to surgery or invasive procedures. British Committee for Standards in Haematology.* Br J Haematol 140*, 496–504.*

7. *Ageno, W., Gallus, A.S., Wittkowsky, A., Crowther, M., Hylek, E.M., Palareti, G. et al. (2012). Oral anticoagulant therapy: Antithrombotic therapy and prevention of thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines.* Chest *141, e44S–88S.*

8. *Clinical and Laboratory Standards Institute. (2004). CLSI EP5-A2. Evaluation of precision performance of quantitative measurement methods.*

The CoaguChek® Pro II system is not available in all markets. Please contact your local Roche representative to obtain the appropriate product information for your country.

Roche Diagnostics International Ltd
CH-6343 Rotkreuz
Switzerland
www.coaguchek.com

CoaguChek®
Because it's my life