CoaguChek™ Systems

FOR COAGUCHEK SYSTEM

Tests

This is a CLIA waived system. These test strips are to be used with the CoaguChek System.

Intended Use

For quantitative prothrombin time (PT) testing in fresh capillary or venous whole blood with the CoaguChek System by professional healthcare providers.

Cat. No. 3116247

48 Test Strips
1 Code Chip

Introduction

Blood coagulation is one of the body's protective responses. Blood clots (thrombi) form as a direct response to vessel injury, preventing excessive loss of blood. Certain disease conditions require oral anticoagulants, sometimes known as blood thinners. Warfarin, which is sometimes known as Coumadin®, is a commonly used anticoagulant. Patients on warfarin must be carefully monitored to ensure the anticoagulant level is maintained in the therapeutic range. One method for monitoring the anticoagulant level is by using the one-stage Prothrombin Time (PT) Test. The CoaguChek Systems Test uses a modified version of this method.

Test Principle

The CoaguChek Systems Test, used as directed with the CoaguChek Monitor, will accurately measure blood PT values. After placing a drop of fresh whole blood on the test strip, the blood is drawn into the reaction chamber and mixed with reagents that cause coagulation to begin. In the test strip, tiny iron particles are mixed with the sample. Alternating magnetic fields cause the iron particles to move within the sample.[1] The endpoint is reached when the blood clot stops the iron particles from moving. The PT result is then displayed by the monitor.[2]

Read the *CoaguChek System User's Manual* for complete instructions. If you have questions, call Point of Care Technical Service Center at 1-800-428-4674, 24 hours a day, 7 days a week.

Reagents

Each test strip contains rabbit thromboplastin, stabilizers, and preservatives.

Precautions and Warnings:

1. For *in vitro* diagnostic use. Do not take internally.
2. Exercise the normal precautions required for handling all blood specimens and laboratory reagents. Follow your facility's infection control guidelines.
3. CoaguChek Systems Tests may be performed with fresh capillary whole blood from a fingerstick or fresh venous whole blood drawn in an anticoagulant-free plastic syringe.
4. Never add more blood to the test strip after the test has begun, or perform another test using the same fingerstick.

Storage and Stability:

- Keep strips in the original sealed foil pouches.
- Store strips in refrigerator at +2°C to +8°C (+36°F to +46°F) until ready to use. Do not freeze. Test strips are stable for 60 days or until the expiration date, whichever comes first, when stored at room temperature (below 32°C or 90°F).
- Remove only the necessary number of foil pouches from the refrigerator needed to perform a test(s). Test strips must be out of the refrigerator for at least five minutes before use.
- Once the foil pouch has been opened, use the strip within four minutes.

Before Testing

Gather the necessary materials:

- CoaguChek Monitor
- CoaguChek Systems Tests
- Test Strip Code Chip
- Alcohol wipe
- Cotton ball

For capillary specimen collection, you will need:

- Lancets
- Lancet device
- CoaguChek Capillary Blood Collection System, Cat. No. 461 (optional)

For venous specimen collection, you will need:

- Plastic syringe free of anticoagulants.
- Syringe needle should be 23 gauge or larger. A 21 gauge or larger needle is recommended.
- Tourniquet

1. If you are using test strips from a new unopened box, you will need to change the Test Strip Code Chip. The first three numbers after the lot symbol on the test strip pouch should match the numbers on the Test Strip Code Chip. To install the Test Strip Code Chip:
   - Turn the monitor off.
   - Remove and discard the old Code Chip, if one is installed.
   - Insert the new Test Strip Code Chip until it snaps into place. Make sure the label side with code number is up.
   - Refer to the *CoaguChek User's Manual* for additional information.
2. Remove foil pouch from refrigerator. Test strips must be out of the refrigerator for at least five minutes before use.
3. *For capillary sample collection:*

   Prepare lancet device according to manufacturer's instructions.
   - Set aside until needed.

   Prepare capillary collection device (optional).
   - Firmly insert end of capillary tube into the capillary bulb. With each new bulb, be sure to completely insert the capillary tube into the bulb.
   - Set aside until needed.
4. *For venous sample collection:*
   - Prepare a plastic syringe that is free of anticoagulants. The sample must be used immediately after collection.
   - Plasma or serum cannot be used as a testing sample.
   - Glass tubes or syringes must not be used.

Testing

The CoaguChek Systems Test uses only fresh capillary or venous, non-anticoagulated whole blood. Depending on the sample collection method, use method A or B as they apply below.

1. Place monitor on a flat, horizontal surface, free of vibrations, before testing.
2. Turn the monitor on. When PERFORM TEST? appears on the display, press the YES button and the instruction INSERT STRIP will appear.
3. Open foil pouch at the tear mark on the side of the pouch and remove test strip.
4. Insert strip into monitor, printed side up. Make sure you insert the test strip in the direction of the printed arrows. You will see the yellow sample target area through the strip. The monitor displays IS THIS A CONTROL? Press the NO button. The monitor then displays PLEASE WAIT. The monitor will warm the strip for about 45 seconds.
5. When monitor displays APPLY SAMPLE prepare to collect the fresh whole blood sample.

Method A - Capillary sample collection

- Clean finger with alcohol wipe or use soap and warm water. Dry finger thoroughly.
- Stick the fingertip by placing the tip of lancet device against the bottom side of the finger and pushing the trigger button. Gently squeeze finger until a hanging drop of blood forms.
- Touch the capillary tube to the blood drop. Fill the capillary tube halfway. Avoid getting air bubbles into the sample. Do not touch the bulb during sample collection. If blood gets into the capillary bulb during sample collection, discard the bulb.
- Put finger over hole at the top of the capillary bulb. When the monitor displays APPLY SAMPLE, hold the capillary tube directly over the sample target area of the test strip. While keeping finger over the hole, gently push down the top of the bulb until the sample has been expelled onto the sample target of the test strip. Make sure the test strip is flat when testing. Make sure the sample touches the channel surrounding the yellow target zone. The entire target area of the test strip must be completely filled.
- Apply sample to test strip within 15 seconds of lancing the fingertip. ***Note:*** Blood may also be applied directly from the finger to the sample target area. The entire target area must be filled completely with one hanging drop of blood.

Method B - Venous sample collection

- When the monitor displays APPLY SAMPLE, draw the venous sample into a plastic syringe free of anticoagulants.
- Discard the first four drops of blood from the needle, then immediately place one drop of blood from syringe needle directly onto the center of the sample target of the test strip. Make sure the test strip is flat when testing. Make sure the sample touches the channel surrounding the yellow target zone. The entire target area of the test strip must be completely filled.

6. When the blood enters the testing area of the strip, the monitor will display TESTING along with a progress bar. Do not add more blood or touch the test strip while TESTING is displayed. The strip should not be disturbed until the monitor displays the PT value.
7. Remove the test strip.
8. The monitor stores the PT value in memory, along with the date and time the test was performed. You may also record the PT value in a log book.
9. Carefully discard lancet and capillary tube or needle and syringe and the used test strip according to proper infection control guidelines.

Expected Results

CoaguChek System test results are displayed in units equivalent to laboratory plasma measurements. Results may be displayed in the International Normalized Ratio (INR=(PT/Median Normal PT)^{ISI}), seconds, % Quick (a unit used mainly by healthcare professionals in Europe), and as a ratio relative to normal (PT/Median Normal PT).

Normal PT levels vary from person to person. The median normal PT (MNPT) from at least 30 healthy, warfarin-free individuals is determined for each lot of reference reagent to which each strip lot is calibrated to 12.0 seconds (or a ratio of 1). This corresponds to an INR of 1.0. The median PT is usually a good approximation of the geometric mean.[3] Patient results in seconds are that which would be expected for a reagent and instrument system with an International Sensitivity Index (ISI) of 2.0. INRs derived from the CoaguChek System are a result of calibration to a plain rabbit brain thromboplastin reagent tested on an optical instrument having an ISI of about 2.0.

The physician must determine the best PT level depending on the reason for anticoagulant treatment and how each individual responds to treatment (based on Prothrombin Time). Each physician should establish expected values for his or her patient population or individual patients.

In the field of prothrombin testing, variations in reaction mixture composition, thromboplastin tissue type, and system sensitivity may cause some variation in results when comparing results from different laboratory methodologies on the same patient.[4]

Unusual Results

If the patient's PT value seems unusually low or high and you have performed the testing procedure correctly, run a control.

If the control is out of the acceptable range, the following can cause unusually low or high results:

- Control used after expiration date.
- Foil pouch opened and strip not used within four minutes.
- Sealed foil pouch stored improperly.
- Foil pouch damaged.
- Maintenance and cleaning procedures have not been followed. See the *CoaguChek System User's Manual* for these procedures.

If the control is in the acceptable range, the system is working properly. If the result does not match the clinical symptoms, repeat the patient test to rule out procedural error. There are many reasons why the patient may demonstrate unusual results. In the field of prothrombin testing, certain drugs may affect PT results by affecting warfarin pharmacology. The potential effect of a drug interaction with warfarin or the effect of underlying diseases (e.g., liver disease, congestive heart failure) must be considered when interpreting a result. Any unexpected results should always be followed up with appropriate coagulation studies and inquiries to define the cause of the unusual result.

Call Point of Care Technical Service Center at 1-800-428-4674, 24 hours a day, if you have any questions.

Quality Control

Quality control testing ensures the user's technique, integrity of the test strips, and performance of the monitor and strips together. Daily control testing is good laboratory practice and required by most states. Always check with the appropriate licensing or accrediting bodies to ensure your quality control program meets the established standards.

Frequency of Testing Requirements-Waived Testing:

• Daily Requirements:

Two levels of Electronic Quality Control or two levels of liquid quality control (Cat. No. 7745) must be tested to verify proper monitor performance.

• Additional Requirements:

1. Two levels of liquid controls must be tested and results must be within the designated range for the following situations:
   - You open a new box of test strips
   - You suspect improper storage or handling of the strips
   - Patient PT results are unusually high or low
2. Two levels of Electronic Quality Control or two levels of liquid quality control must be tested if the monitor is dropped or mishandled.

The results must be within the designated range.

Frequency of Testing Requirements-Moderate Complexity Testing

Daily quality control testing is good laboratory practice. It is also required by most states and by CLIA '88 regulations. Check with the appropriate licensing or accrediting bodies to ensure that your quality control program meets established standards.

• Daily Requirements

A two level Electronic Quality Control device (Cat. No. 2032155) or Liquid Quality Controls may be tested to verify proper monitor performance.

• Additional Requirements

A Liquid Quality Control (Level 1 or 2) should be tested when:

1. A new shipment of test strips is received
2. A new lot number of strips is opened
3. Improper storage or handling of the strips is suspected
4. Patient PT results are unusually high or low

This testing is in addition to the daily EQC testing. The results must be within the designated ranges.

Be sure to use the appropriate controls for your system: CoaguChek System—Use Cat. No. 7745.

The CoaguChek System Controls are available from your local CoaguChek System dealer or from Roche Diagnostics.

Control tests are performed in a similar way as blood tests, using the CoaguChek System Control instead of blood. The control instructions should be read before using the controls. The system is working properly if the control value displayed by the monitor is within the acceptable range for the control solution tested. The acceptable control range can be found in the control package on the *CoaguChek System Control Values Sheet*. If the value is not acceptable, see the CoaguChek Control package insert instructions. Call Point of Care Technical Service Center at 1-800-428-4674, 24 hours a day, 7 days a week if you have any questions.

Limitations of Procedure

The CoaguChek Systems Test uses only fresh, capillary or venous whole blood. Plasma or serum cannot be used.

Use only plastic syringes without anticoagulants or additives. Glass tubes or syringes must not be used.

The blood drop must be a minimum of 10 µL in volume. Low sample volume will cause a SAMPLE ERROR - REMOVE STRIP warning.

This test measures PT results in persons on warfarin-type (Coumadin®) therapy. This test should not be used to monitor persons on heparin therapy. *In vitro* studies showed the CoaguChek Systems Tests are sensitive to levels of heparin over 0.15 U/mL.

When a patient is on intravenous infusion therapy, do not collect sample from arm receiving infusion line.

Hematocrit ranges between 32-52% do not significantly affect test results.

No interference was found in lipemic samples containing up to 500 mg/dL of triglycerides. Testing performed with *in vitro*-spiked samples indicated bilirubin up to 20 mg/dL and hemolysis up to 500 mg/dL did not significantly affect test results.

The presence of anti-phospholipid antibodies (APAs) such as Lupus antibodies (LA) can potentially lead to prolonged clotting times, i.e., elevated INR values. A comparison to an APA-insensitive laboratory method is recommended if the presence of APAs is known or suspected.[5]

Sources of error

If problems occur when performing tests, please check the following:

- Have you used a wrong Test Strip Code Chip? The first three numbers after the lot symbol on the test strip pouch should match the numbers on the Test Strip Code Chip.
- The test result may be affected by hematocrit values outside the range 32% to 52%.
- In rare cases, patients with long clotting times (>8 INR, >33.9 sec) may produce a test error. If test errors persist, results must be confirmed with an alternative test method. Contact the patient's physician.
- Have you performed the test in accordance with the User's Manual and this package insert?
- Have you used correctly stored test strips (see "Storage and Stability")?
- Have you moved the test strip between sample application and the display of the result? Do not touch or move the test strip after having applied the drop of blood. Also, do not attempt to apply additional blood to the test strip once a first drop has been applied (no double-dosing). In either case the monitor displays an error message and a measurement with a new test strip will be necessary.
- Are the test strip guide and the door clean?

Performance Characteristics

Verified Clinical Range: In clinical trials, patients tested in the 9.6 to 33.9 second range (0.6 to 8.0 INR). Performance outside this range has not been verified.

Sensitivity: The CoaguChek System is sensitive to deficiencies of Factors II, V, VII, and X.

Accuracy: The CoaguChek System was compared against the CoaguChek Plus Protime Test System and the MLA 700 Analyzer. The following accuracy data was obtained:

INR Scale	*Seconds Scale*
Capillary Whole Blood	**Capillary Whole Blood**
CoaguChek vs. CoaguChek Plus	CoaguChek vs. CoaguChek Plus
n = 81	n = 81
y = 0.864x - 0.002	y = 0.945x - 0.1
r = 0.966	r = 0.970
Venous Whole Blood	**Venous Whole Blood**
CoaguChek vs. CoaguChek Plus	CoaguChek vs. CoaguChek Plus
n = 81	n = 81
y = 1.022x - 0.2	y = 1.033x - 0.8
r = 0.952	r = 0.962
Capillary Whole Blood	**Capillary Whole Blood**
CoaguChek vs. MLA 700 Plasma Reference	CoaguChek vs. MLA 700 Plasma Reference
n = 81	n = 81
y = 0.793x + 0.2	y = 0.825x + 1.6
r = 0.983	r = 0.985
Venous Whole Blood	**Venous Whole Blood**
CoaguChek vs. MLA 700 Plasma Reference	CoaguChek vs. MLA 700 Plasma Reference
n = 81	n = 81
y = 0.862x + 0.2	y = 0.859x + 1.3
r = 0.984	r = 0.985
CoaguChek	**CoaguChek**
Venous vs. Capillary	Venous vs. Capillary
n = 81	n = 81
y = 1.077x - 0.07	y = 1.036x - 0.2
r = 0.992	r = 0.995

Precision:

Within-Day

	Commercial Control Material			
	INR Scale		Seconds Scale	
	Level 1	*Level 2*	*Level 1*	*Level 2*
n	20	20	20	20
Mean	1.03	3.66	12.24	23.01
SD	0.05	0.48	0.33	1.43
CV%	4.56	12.98	2.70	6.23

Day-To-Day

	Commercial Control Material			
	INR Scale		Seconds Scale	
	Level 1	*Level 2*	*Level 1*	*Level 2*
n	20	20	20	20
n	48	48	48	48
Mean	1.07	3.72	12.56	23.19
SD	0.07	0.31	0.47	0.94
CV%	6.66	8.41	3.71	4.06

	Whole Blood (Precision of Patient Duplicate Measurements)			
	INR Scale		Seconds Scale	
	Capillary	*Venous*	*Capillary*	*Venous*
n	81	81	81	81
Mean	2.16	2.26	17.2	17.6
SD	0.11	0.10	0.37	0.33
CV%	5.23	4.44	2.17	1.89

Return Policy

If there is a problem with the CoaguChek Systems Tests, you may be asked to return them, along with the Test Strip Code Chip, to Roche Diagnostics. Before returning, call the Point of Care Technical Service Center at 1-800-428-4674. You will be mailed a return authorization label which must be put on the shipping carton. Packages received without this label will be returned at your expense.

References

1 Plonsey R, Collin RE. Magnetic field in material bodies. In: Principles and applications of electromagnetic fields. New York: McGraw-Hill Book Co., p. 226-57, 1961.

2 Oberhardt BJ, Taylor M, Alkadi ZY, Dermott SC. Diagnostic assay system for convenient monitoring of oral anticoagulant therapy (Abstract). *Thromb Haemostas*, 1989;62:327.

3 Loeliger EA, van den Besselaar AMHP and Lewis SM., Reliability and clinical impact of the normalization of the prothrombin times in oral anticoagulant control. *Thromb Haemostas*, 1985;53:148-154.

4 Kaatz SS, White RH, Hill J, Mascha E, Humphries JE, and Becker DM, "Accuracy of Laboratory and Portable Monitor International Normalization Ratio Determinations." *Arch. Intern. Med.* 1995;155:1861-1867.

5 Moll, S. and Ortel, TL "Monitoring Warfarin Therapy in Patients with Lupus Anticoagulants." *Annals of Internal Medicine* 1997;127:177-185.

Additional Information

Refer to the *CoaguChek User's Manual* for additional information about your system.

If you still have questions, call Point of Care Technical Service Center at 1-800-428-4674, 24 hours a day, 7 days a week.

This system (monitor and test strips) and its use are covered by one or more of the following U.S. Patents: 4,849,340; 5,110,727; 5,164,598; 5,300,779; 5,522,255; 5,686,659; 5,710,622; 5,789,664; 5,792,944; 5,832,921; 5,886,252 and Des. 361,129.

The test strips are covered by U.S. Patent No. 5,488,816; and 5,975,153.

COAGUCHEK is a trademark of a Member of the Roche Group.

Coumadin is a trademark of DuPont Pharmaceutical Company.

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CoaguChek™ Systems

FOR COAGUCHEK S SYSTEM

Tests

This is a CLIA waived system. These test strips are to be used with the CoaguChek S System.

Intended Use
The CoaguChek System is intended for quantitative prothrombin time (PT) testing for monitoring of warfarin therapy, using fresh capillary or venous whole blood by professional healthcare providers.

Cat. No. 3116247

48 Test Strips
1 Code Chip

Introduction
Blood coagulation is one of the body's protective responses. Blood clots (thrombi) form as a direct response to vessel injury, preventing excessive loss of blood. Certain disease conditions require oral anticoagulants, sometimes known as blood thinners. Warfarin, which is sometimes known as Coumadin®, is a commonly used anticoagulant. Patients on warfarin must be carefully monitored to ensure the anticoagulant level is maintained in the therapeutic range. One method for monitoring the anticoagulant level is by using the one-stage Prothrombin Time (PT) Test. The CoaguChek Systems Test uses a modified version of this method.

Test Principle
The CoaguChek Systems Test, used as directed with the CoaguChek S System Monitor, will accurately measure blood PT values. After placing a drop of fresh whole blood on the test strip, the blood is drawn into the reaction chamber and mixed with reagents that cause coagulation to begin. In the test strip, tiny iron particles are mixed with the sample. Alternating magnetic fields cause the iron particles to move within the sample.[1] The endpoint is reached when the blood clot stops the iron particles from moving. The PT result is then displayed by the monitor.[2]

Read the *CoaguChek S System User's Manual* for complete instructions. If you have questions, call Point of Care Technical Service Center at 1-800-428-4674, 24 hours a day, 7 days a week.

Reagents
Each test strip contains rabbit thromboplastin, stabilizers, and preservatives. Refer to the *Expected Results* Section for ISI information.

Precautions and Warnings:

1. For *in vitro* diagnostic use. Do not take internally.
2. Exercise the normal precautions required for handling all blood specimens and laboratory reagents. Follow your facility's infection control guidelines.
3. CoaguChek Systems Tests may be performed with fresh capillary whole blood from a fingerstick or fresh venous whole blood drawn in an anticoagulant-free plastic syringe.
4. Never add more blood to the test strip after the test has begun, or perform another test using the same fingerstick.

Storage and Stability:

- Keep strips in the original sealed foil pouches.
- Store strips in refrigerator at +2°C to +8°C (+36°F to +46°F) until ready to use. Do not freeze. Test strips are stable for 60 days or until the expiration date, whichever comes first, when stored at room temperature (below 32°C or 90°F).
- Remove only the necessary number of foil pouches from the refrigerator needed to perform a test(s). Allow at least five minutes for the sealed pouch to reach room temperature before opening the foil pouch for testing.
- Once the foil pouch has been opened, use the strip within four minutes.

Before Testing
Gather the necessary materials:

- CoaguChek S System Monitor
- CoaguChek Systems Tests
- Test Strip Code Chip
- Alcohol wipe
- Cotton ball

For capillary specimen collection, you will need:

- Lancets
- Lancet device
- CoaguChek Capillary Blood Collection System, Cat. No. 461 (optional)

For venous specimen collection, you will need:

- Plastic syringe free of anticoagulants
- Syringe needle should be 23 gauge or larger. A 21 gauge or larger needle is recommended.
- Tourniquet

1. If you are using test strips from a new unopened box, you will need to change the Test Strip Code Chip. The first three numbers after the lot symbol on the test strip pouch should match the numbers on the Test Strip Code Chip. To install the Test Strip Code Chip, follow the instructions in your User's Manual.
2. Remove foil pouch from refrigerator and allow at least five minutes to reach room temperature (18-32ºC or 65-90ºF) before opening and performing a test.
3. For capillary sample collection:
   - Prepare lancet device according to manufacturer's instructions.
     - Set aside until needed.
   - Prepare capillary collection device (optional).
     - Firmly insert end of capillary tube into the capillary bulb. With each new bulb, be sure to completely insert the capillary tube into the bulb.
     - Set aside until needed.
4. For venous sample collection:
   - Prepare a plastic syringe that is free of anticoagulants. The sample must be used immediately after collection.
     - Plasma or serum cannot be used as a testing sample.
     - Glass tubes or syringes must not be used.

Testing
The CoaguChek Systems Test uses only fresh capillary or venous, non-anticoagulated whole blood. Depending on the sample collection method, use method A or B as they apply below.

Monitor should be on a flat surface, free of vibrations, when testing

1. Turn the monitor on. Follow the prompts to insert a strip.
2. Open the foil pouch at the tear mark on the side and remove the test strip.
3. Insert the strip into the monitor, printed side up, and push it in until it stops.
4. Wait until you are prompted to apply the sample.
5. Prepare to collect the fresh whole blood.

Method A - Capillary sample collection

- Clean finger with alcohol wipe or use soap and warm water. Dry finger thoroughly.
- Stick the fingertip by placing the tip of lancet device against the bottom side of the finger and pushing the trigger button. Gently squeeze finger until a hanging drop of blood forms.
- Touch the capillary tube to the blood drop. Fill the capillary tube halfway. Avoid getting air bubbles into the sample. Do not touch the bulb during sample collection. If blood gets into the capillary bulb during sample collection, discard the bulb.
- Put finger over hole at the top of the capillary bulb. When the monitor prompts for sample application, hold the capillary tube directly over the sample target area of the test strip. While keeping finger over the hole, gently push down the top of the bulb until the sample has been expelled onto the sample target of the test strip. Make sure the test strip is flat when testing. Make sure the sample touches the channel surrounding the target zone. The entire target area of the test strip must be completely filled.
- Apply sample to test strip within 15 seconds of lancing the fingertip. ***Note:*** Blood may also be applied directly from the finger to the sample target area. The entire target area must be filled completely with one hanging drop of blood.

Method B - Venous sample collection

- When the monitor prompts for sample application, draw the venous sample into a plastic syringe free of anticoagulants.
- Discard the first four drops of blood from the needle, then immediately place one drop of blood from syringe needle directly onto the center of the sample target of the test strip. Make sure the test strip is flat when testing. Make sure the sample touches the channel surrounding the target zone. The entire target area of the test strip must be completely filled.

6. When the blood enters the testing area of the strip, the monitor enters the testing mode. Do not add more blood or touch the test strip during testing. The strip should not be disturbed until the monitor displays the PT result.
7. Remove the test strip.
8. The monitor stores the PT value in memory, along with the date and time the test was performed.
9. Carefully discard lancet and capillary tube or needle and syringe and the used test strip properly, according to infection control guidelines.

Expected Results
The CoaguChek S System Monitor displays test results in units equivalent to laboratory plasma measurements. Results may be displayed in the International Normalized Ratio (INR=PT/Mean Normal PT)*, seconds, % Quick (a unit used mainly by health care professionals in Europe), and as a ratio relative to normal (PT/Median Normal PT).

Normal PT levels vary from person to person. When the CoaguChek Systems Test was performed using the CoaguChek S Monitor on 123 normal, healthy, coumarin-free individuals, using venous samples, 95% of the prothrombin times ranged from 10.6 to 13.4 seconds. A subset of these individuals (n=17), using capillary blood, gave results ranging from 10.4 to 12.5 seconds. For the purpose of calculating INR or ratio values, normal is defined as 12.0 seconds. This corresponds to an INR of 1.0. The ISI of the system is defined as 2.0.

The physician must determine the best PT level depending on the reason for anticoagulant treatment and how each individual responds to treatment (based on Prothrombin Time). Each physician should establish expected values for his or her patient population or individual patients.

In the field of prothrombin testing, variations in reaction mixture composition, thromboplastin tissue type, and system sensitivity may cause some variation in results when comparing results from different laboratory methodologies on the same patient.[3]

Unusual Results
If the patient's PT value seems unusually low or high and you have performed the testing procedure correctly, run liquid controls as described in the *Quality Control* section below.

If the controls are out of the acceptable range, the following can cause unusually low or high results:

- Control used after expiration date.
- Foil pouch opened and strip not used within four minutes.
- Sealed foil pouch stored improperly.
- Foil pouch damaged.
- Maintenance and cleaning procedures have not been followed. See the *CoaguChek S System User's Manual* for these procedures.

If the controls are in the acceptable range, the system is working properly. If the result does not match the clinical symptoms, repeat the patient test to rule out procedural error. There are many reasons why the patient may demonstrate unusual results. In the field of prothrombin testing, certain drugs may affect PT results by affecting warfarin pharmacology. The potential effect of a drug interaction with warfarin or the effect of underlying diseases (e.g., liver disease, congestive heart failure) must be considered when interpreting a result. Any unexpected results should always be followed up with appropriate coagulation studies and inquiries to define the cause of the unusual result.

Call Point of Care Technical Service Center at 1-800-428-4674, 24 hours a day, 7 days a week if you have any questions.

Quality Control
Quality control testing ensures the user's technique, integrity of the test strips, and performance of the monitor and strips together.

Frequency of Testing Requirements-Waived Testing

• Daily Requirements:

Two levels of Electronic Quality Control (EQC) or two levels of liquid quality control must be tested to verify proper monitor performance.

• Additional Requirements:

1. Two levels of liquid controls must be tested and results must be within the designated range for the following situations:
   - You open a new box of test strips
   - You suspect improper storage or handling of the strips
   - Patient PT results are unusually high or low
2. Two levels of Electronic Quality Control or two levels of liquid quality control must be tested if the monitor is dropped or mishandled.

The results must be within the designated range.

Frequency of Testing Requirements-Moderate Complexity Testing

Daily quality control testing is good laboratory practice. It is also required by most states and by CLIA '88 regulations. Check with the appropriate licensing or accrediting bodies to ensure that your quality control program meets established standards.

• Daily Requirements

A two level Electronic Quality Control device (Cat. No. 2032155) or Liquid Quality Controls may be tested to verify proper monitor performance.

• Additional Requirements

A Liquid Quality Control (Level 1 or 2) should be tested when:

1. A new shipment of test strips is received
2. A new lot number of strips is opened
3. Improper storage or handling of the strips is suspected
4. Patient PT results are unusually high or low

This testing is in addition to the daily EQC testing. The results must be within the designated ranges.

Be sure to use the appropriate controls for your system:
CoaguChek S System - Use Cat. No. 3033384

CoaguChek S System Controls are available from your local CoaguChek S System dealer or from Roche Diagnostics.

Control tests are performed in a similar way as blood tests, using the CoaguChek S System Control instead of blood. The control instructions should be read before using the controls. The system is working properly if the control value displayed by the monitor is within the acceptable range for the control solution tested. The acceptable control range can be found in the control package on the *Control Value Sheet.* If the value is not acceptable, see the CoaguChek S System Control package insert instructions. Call Point of Care Technical Service Center at 1-800-428-4674, 24 hours a day, 7 days a week if you have any questions.

Limitations of Procedure
The CoaguChek Systems Test uses only fresh, capillary or venous whole blood. Plasma or serum cannot be used.

Use only plastic syringes without anticoagulants or additives. Glass tubes or syringes must not be used.

The blood drop must be a minimum of 10 µL in volume. Low sample volume will cause an error message.

This test measures PT results in persons on warfarin-type (Coumadin®) therapy. This test should not be used to monitor persons on heparin therapy. *In vitro* studies showed the CoaguChek Systems Tests are sensitive to levels of heparin over 0.15 U/mL.

When a patient is on intravenous infusion therapy, do not collect sample from arm receiving infusion line.

Hematocrit ranges between 32-52% do not significantly affect test results.

No interference was found in lipemic samples containing up to 500 mg/dL of triglycerides. Testing performed with *in vitro*-spiked samples indicated bilirubin up to 20 mg/dL and hemolysis up to 500 mg/dL did not significantly affect test results.

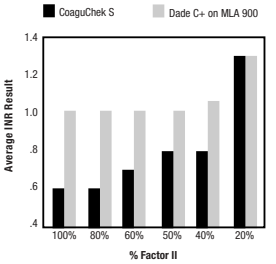
The presence of anti-phospholipid antibodies (APAs) such as Lupus antibodies (LA) can potentially lead to prolonged clotting times, i.e., elevated INR values. A comparison to an APA-insensitive laboratory method is recommended if the presence of APAs is known or suspected.[5]

Sources of error
If problems occur when performing tests, please check the following:

- Have you used a wrong Test Strip Code Chip? The first three numbers after the lot symbol on the test strip pouch should match the numbers on the Test Strip Code Chip.
- The test result may be affected by hematocrit values outside the range 32% to 52%.
- In rare cases, patients with long clotting times (>8 INR, >33.9 sec) may produce a test error, as indicated by ⚠ ERROR and a flashing test strip icon. If test errors persist, results must be confirmed with an alternative test method. Contact the patient's physician.
- Have you performed the test in accordance with the User's Manual and this package insert?
- Have you used correctly stored test strips (see "Storage and Stability")?
- Have you moved the test strip between sample application and the display of the result? Do not touch or move the test strip after having applied the drop of blood. Also, do not attempt to apply additional blood to the test strip once a first drop has been applied (no double-dosing). In either case the monitor displays an error message and a measurement with a new test strip will be necessary.
- Are the test strip guide and the door clean?

Performance Characteristics
Measuring Range: The CoaguChek S System has a PT reportable range of 0.6 to 8.0 INR and 9.6 to 33.9 seconds (sec).

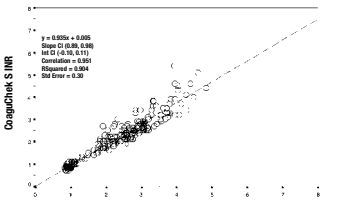
Sensitivity: Internal studies were performed utilizing four replicates of each Factor Level. Samples were assayed on the CoaguChek S System and Dade C Plus on the MLA 900 Analyzer. The results are shown in the following graphs.



Accuracy: 219 venous samples were collected from outpatients at three external sites. The INR of each sample was compared to the INR of a venous plasma sample measured on MLA 700/1600 Analyzers, using Dade C+ reagent. The patient clinical conditions included (number of patients): normal (55), atrial fibrillation (35), valve replacement (36), stroke/TIA (24), DVT (14), other heart-related disorders (32), other clotting disorders (23).

Site	N	Slope	Slope Conf. Int.	Intercept (INR)	Intercept Conf. Int.	Correlation
1	78	0.909	(0.85, 0.97)	0.04	(-0.13, 0.21)	0.956
2	69	0.990	(0.91, 1.07)	-0.07	(-0.27, 0.14)	0.946
3	72	0.919	(0.85, 0.99)	0.02	(-0.15, 0.19)	0.954
Combined	219	0.935	(0.89, 0.98)	0.005	(-0.10, 0.11)	0.951

CoaguChek S Venous Data from All Sites
Lot 1 vs Dade C+ on MLA Analyzers (N=219)



High INR Accuracy: Additional studies were performed at two sites to collect high INR data (>6.0 INR). Site 4 used two different CoaguChek S Monitors and two different lot numbers of test strips to test venous samples. Site 5 used two different CoaguChek S Monitors and one lot number of test strips to test venous samples. A single venipuncture was used to obtain duplicate results. Site 5 also performed capillary blood testing using a single fingerstick and one CoaguChek S Monitor. At each site a patient's sample was collected by the same operator. The INR of each sample was compared to the INR of venous plasma samples measured on an MLA 900 Analyzer. The patient clinical conditions included (number of patients): valve replacement (6), stroke (1), and other heart-related disorders (1).

There is generally better agreement among prothrombin time methods within the therapeutic range (<3-4 INR) and poorer agreement at higher INRs.[4] The precision and accuracy of CoaguChek S System diminish above an INR of 6.0.

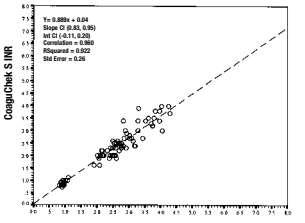
	Site	Result 1	Result 2	Dade C+ Method	Dade Innovin Method 2	Coagu-Chek S 1 vs Coagu-Chek S 2	Coagu-Chek S 1 vs Plasma Method 1	Coagu-Chek S 2 vs Plasma Method 1	Plasma Method 1 vs Plasma Method 2
Venous	4	5.2 (lot 1)	6.3 (lot 2)	5.9	5.2	1.1	-0.7	0.4	0.7
	4	5.8 (lot 1)	6.1 (lot 2)	7.6	6.3	0.4	-1.1	-1.6	1.3
	4	4.7 (lot 2)		6.2	5.2		-1.5		1.0
	4	5.3 (lot 2)	6.0 (lot 4)	5.9	7.2	1.9	-0.6	1.1	0.1
	4	7.1 (lot 3)	8.7 (lot 4)	7.7	7.5	1.6	-0.6	1.0	0.2
	5	8.5 (lot 3)	8.2 (lot3)	7.9	6.1	0	0.6	0.6	1.8
	5	8.4 (lot 3)	6.9 (lot 3)	4.7	4.4	0.1	1.7	1.8	0.3
	5	>9.3 (lot 3)	>9.3 (lot 3)	7.6	6.3	0	>1.5	>1.5	1.3
Capillary	5	8.7 (lot 3)		7.9	6.1		0.8		1.8
	5	8.5 (lot 3)		4.7	4.4		1.8		0.3
	5	>9.3 (lot 3)		7.6	6.3		>1.5		1.3

(1)Results are shaded if INR = 6.0 - 8.0
(2)Results are shaded if difference > 0.5 INR

Seventy-eight paired capillary and venous samples were collected at one external site. Capillary blood samples were assayed on the CoaguChek S Monitor with CoaguChek Systems Tests and venous plasma samples were measured on an MLA 700 Analyzer with Dade® C+ reagent. The results comparison is as follows:

Site	N	Slope	Slope Conf. Int.	Intercept (INR)	Intercept Conf. Int.	Correlation
1	78	0.889	(0.83, 0.95)	0.04	(-0.11, 0.20)	0.960

CoaguChek S Capillary Data from Site 1
Lot 1 vs Dade C+ on MLA 700 (N=78)



Precision: Whole blood imprecision for venous samples was determined from sample duplicates, at three external sites. For capillary blood, the data was collected from sample duplicates, using a single fingerstick, at one external site. The following data was obtained and the analysis was performed using a one-factor ANOVA model:

Sample Type	Site	N	Mean* (Sec)	SD* (Sec)	CV* (%)	Mean* (INR)	SD* (INR)	CV* (%)
Capillary-normal	1	17	11.6	0.37	3.23	0.9	0.08	8.66
Capillary-therapeutic	1	54	19.4	0.43	2.21	2.6	0.13	4.91
Venous-normal	1	17	11.7	0.35	2.98	0.9	0.07	7.83
	2	19	11.8	0.24	2.01	0.9	0.06	6.49
	3	17	11.9	0.38	3.23	1.0	0.08	8.63
	Combined	53	11.8	0.33	2.76	0.9	0.07	7.67
Venous-therapeutic	1	54	19.7	0.56	2.84	2.7	0.16	6.09
	2	50	19.1	0.40	2.10	2.6	0.12	4.80
	3	51	19.0	0.59	3.11	2.5	0.17	6.66
	Combined	155	19.3	0.52	2.73	2.6	0.15	5.91

*** Testing was performed in duplicate; therefore, "mean" refers to the mean of samples.**

*** "SD" and "CV" are the SD and CV of the replicates.**

The monitor-to-monitor, lot-to-lot, and strip-to-strip variability was assessed during internal studies which used two levels of liquid controls, with three test strip lots across nine CoaguChek S Monitors. The following data was obtained:

Level 1

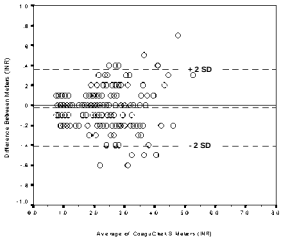
	Mean	15.0	Mean	1.5
	Seconds		INR	
	SD	CV	SD	CV
Lot-to-Lot	0.58	3.9%	0.10	6.4%
Monitor-to-Monitor	0.21	1.4%	0.04	2.6%
Strip-to-Strip	0.54	3.6%	0.12	7.5%
Total	0.82	5.5%	0.16	10.2%

Level 2

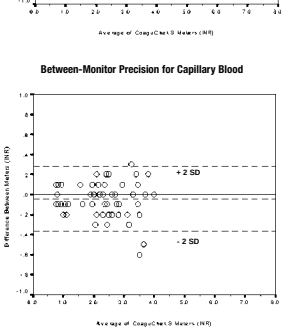
	Mean	23.1	Mean	3.7
	Seconds		INR	
	SD	CV	SD	CV
Lot-to-Lot	1.03	4.5%	0.32	8.8%
Monitor-to-Monitor	0.70	3.0%	0.23	6.4%
Strip-to-Strip	1.14	5.0%	0.39	10.5%
Total	1.69	7.3%	0.55	15.1%

Between-Monitor Precision: The following charts represent between-monitor precision for capillary and venous blood.

Between-Monitor Precision for Venous Blood



Between-Monitor Precision for Capillary Blood



Return Policy
If there is a problem with the CoaguChek Systems Tests, you may be asked to return them, along with the Test Strip Code Chip, to Roche Diagnostics. Before returning, call the Point of Care Technical Service Center at 1-800-428-4674. You will be mailed a return authorization label which must be put on the shipping carton. Packages received without this label will be returned at your expense.

References

1 Plonsey R, Collin RE. Magnetic field in material bodies. In: Principles and applications of electromagnetic fields. New York: McGraw-Hill Book Co., p. 226-57, 1961.

2 Oberhardt BJ, Taylor M, Alkadi ZY, Dermott SC. Diagnostic assay system for convenient monitoring of oral anticoagulant therapy [Abstract]. *Thromb Haemostas*, 1989;62:327.

3 Loeliger EA, van den Besselaar AMHP and Lewis SM., Reliability and clinical impact of the normalization of the prothrombin times in oral anticoagulant control. *Thromb Haemostas*, 1985;53:148-154.

4 Kaatz SS, White RH, Hill J, Mascha E, Humphries JE, and Becker DM, "Accuracy of Laboratory and Portable Monitor International Normalization Ratio Determinations." *Arch. Intern. Med.* 1995;155:1861-1867.

5 Moll, S. and Ortel, TL "Monitoring Warfarin Therapy in Patients with Lupus Anticoagulants." *Annals of Internal Medicine* 1997;127:177-185.

Additional Information
Refer to the *CoaguChek S User's Manual* for additional information about your system.

If you still have questions, call Point of Care Technical Service Center at 1-800-428-4674, 24 hours a day, 7 days a week.

The CoaguChek S System (monitor and test strips) and its use are covered by one or more of the following U.S. Patents: 4,849,340; 5,110,727; 5,164,598; 5,300,779; 5,522,255; 5,710,622; 5,789,664; 5,792,944; and 5,886,252.

The test strips are covered by U.S. Patent No. 5,488,816 and 5,975,153.

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