D-Dimer Test Product Insert
Rapid quantitative test for D-Dimer.
INTENDED USE
The Quidel Triage D-Dimer Test is a fluorescence immunoassay to be used with the Quidel Triage Meters for the quantitative determination of cross-linked fibrin degradation products containing D-dimer in EDTA anticoagulated whole blood and plasma specimens. The test is used as an aid in the assessment and evaluation of patients suspected of having disseminated intravascular coagulation or thromboembolic events including pulmonary embolism.

SUMMARY AND EXPLANATION OF THE TEST
During the coagulation process, thrombin converts fibrinogen to soluble fibrin by the proteolytic removal of both fibrinopeptide A and fibrinopeptide B. Soluble fibrin spontaneously polymerizes, and the D regions are covalently cross-linked through a process that is catalyzed by factor Xlla. Cross-linked fibrin is ultimately degraded via the fibrinolytic pathway. Plasmin cleaves bonds in the cross-linked fibrin lattice and liberates fibrin degradation products (FDPs), including a 200 kDa cross-link of two fragment D molecules (D-dimer). Elevations of circulating D-dimer have been described in patients with venous thromboembolism, including pulmonary embolism (PE) and deep venous thrombosis (DVT) (see Goldhaber, S.Z. (1998) New Engl. J. Med. 339, 93-104).

PRINCIPLES OF THE PROCEDURE
The Quidel Triage D-Dimer Test is a single use fluorescence immunoassay device designed to determine the concentration of D-dimer in EDTA anticoagulated whole blood or plasma specimens. The test procedure involves the addition of several drops of an EDTA anticoagulated whole blood or plasma specimen to the sample port on the Test Device. After addition of the specimen, the whole blood cells are separated from the plasma using a filter contained in the Test Device. The specimen reacts with fluorescent antibody conjugates and flows through the Test Device by capillary action. Complexes of each fluorescent antibody conjugate are captured on a discrete zone resulting in a binding assay.

The Test Device is inserted into the Quidel Triage Meters (hereafter referred to as Meter). The Meter is programmed to perform the analysis after the specimen has reacted with the reagents within the Test Device. The analysis is based on the amount of fluorescence the Meter detects within a measurement zone on the Test Device. The concentration of the analyte in the specimen is directly proportional to the fluorescence detected. The results are displayed on the Meter screen in approximately 20 minutes from the addition of specimen. All results are stored in the Meter memory to display or print when needed. If connected, the Meter can transmit results to the lab or hospital information system.
REAGENTS AND MATERIALS PROVIDED
The Test Device contains all the reagents necessary for the quantification of cross-linked fibrin degradation products containing D-dimer in EDTA anticoagulated whole blood or plasma specimens. The Test Device contains:

- Murine monoclonal antibodies against D-dimer
- Fluorescent dye
- Stabilizers.

Kit contains:

<table>
<thead>
<tr>
<th>Component</th>
<th>Quantity</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>TEST DEVICE</strong></td>
<td>25</td>
<td>Test Devices</td>
</tr>
<tr>
<td></td>
<td>25</td>
<td>Transfer Pipettes</td>
</tr>
<tr>
<td>Reagent CODE CHIP™ Module</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Printer Paper Roll</td>
<td>1</td>
<td></td>
</tr>
</tbody>
</table>

Materials Required but Not Provided
Quidel Triage MeterPro Cat. # 55070 or 55071
Triage MeterPlus Cat. # 55040 or 55041
Quidel Triage Total 5 Control 1 Cat. # 88753
Quidel Triage Total 5 Control 2 Cat. # 88754

WARNINGS AND PRECAUTIONS
- For In Vitro Diagnostic Use.
- For use by healthcare professionals.
- Do not use the kit beyond the expiration date printed on the outside of the box.
- Carefully follow the instructions and procedures described in this insert.
- Optimal results will be achieved by performing testing at temperatures between 20°C to 24°C (68°F to 75°F).
- Keep the Test Device in the sealed pouch until ready for immediate use. Discard after single use.
- The transfer pipette should be used for one patient specimen only. Discard after single use.

- Sample dilution is not recommended.
- The use of non-Quidel Controls or Calibration Verification materials is not recommended.
- Patient specimens, used Test Devices and used transfer pipettes may be potentially infectious. Proper handling and disposal methods should be established by the laboratory in accordance with local, state, and federal regulations.
- Proper laboratory safety techniques should be followed at all times when working with patient specimens because they are potentially infectious.
- The Quidel Triage D-Dimer Test should not be used as absolute evidence for PE or DVT. As with all in vitro diagnostic tests, the test results should be interpreted by the physician in conjunction with clinical findings and other test results.

STORAGE AND HANDLING REQUIREMENTS
- Store the Test Devices in a refrigerator at 2°C to 8°C (35°F to 46°F).
- Once removed from refrigeration, the pouched Test Device is stable for up to 14 days at room temperature, but not beyond the expiration date printed on the pouch. With a soft, felt tip marker, gently write the date and time of removal from the refrigerator on the pouch and cross out the manufacturer expiration date printed on the pouch. Care must be taken to document the time the product is at room temperature. Once equilibrated to room temperature, do not return the Test Device to refrigeration.
- Before using refrigerated Test Devices, allow individual foil pouches to reach operating temperature (20°C to 24°C or 68°F to 75°F). This will take a minimum of 15 minutes. If a kit containing multiple Test Devices is being removed from refrigeration, allow the kit to reach room temperature before use. This will take a minimum of 60 minutes.
- Do not remove the Test Device from the pouch until prepared for immediate use.

SPECIMEN COLLECTION AND PREPARATION
- A venous whole blood or plasma specimen using EDTA as the anticoagulant is required for testing with this product. Specifically, plastic K2 EDTA tubes are recommended for sample collection to ensure optimal product performance. Other blood specimen types, draw methods or anticoagulants have not been evaluated.
- For specimen collection, follow the sample tube manufacturer’s recommended procedure.
- If using whole blood, test patient specimen within 24 hours of sample collection. If testing cannot be completed within 24 hours, the plasma should be separated and stored at -20°C until it can be tested. No more than a single freeze/thaw cycle is recommended.
- Transport specimens at room temperature or chilled and avoid extreme temperatures.
- Avoid using severely hemolyzed specimens whenever possible. If a specimen appears to be severely hemolyzed, another specimen should be obtained and tested.
TEST PROCEDURE
Lot Calibration Using the Reagent CODE CHIP Module
When a new lot of Test Devices is opened, the calibration and expiration data for that lot of Test Devices must be transferred to the Meter before patient testing. Use the Reagent CODE CHIP module supplied with the new lot of Test Devices to transfer the data to the Meter.

Perform one time for each new lot of Test Devices
1. From the main screen, select Install New Code Chip. Press Enter.
2. Place the Reagent CODE CHIP module into the lower left front corner of the Meter and follow the prompts on the screen.
3. Remove the Reagent CODE CHIP module from the Meter when data transfer is complete.
4. Place the Reagent CODE CHIP module back into its original container for storage.

Testing Patient Samples
Procedural Notes
- For each day of patient testing, perform QC Device testing. Refer to the Quality Control Considerations section.
- Frozen plasma and refrigerated whole blood or plasma specimens must be allowed to reach room temperature and be mixed thoroughly before testing.
  - Mix whole blood specimens by gently inverting the tube several times.
  - Mix plasma specimens by vortexing or inverting the tube several times.

Step 1 – Add Patient Specimen
1. Open the pouch and label the Test Device with the patient identification number.
   NOTE: Do not use fluorescent or brightly colored ink, or write outside of the blank area as this may interfere with the test.
2. Place the Test Device on a level, horizontal surface.
3. Using the transfer pipette, squeeze the larger (top) bulb completely and insert the tip into the specimen.
   NOTE: Ensure that the pipette is not under filled or over filled. An under filled pipette is one where the barrel is not filled completely with specimen and there is no specimen in the lower bulb. An over filled pipette is one where there is some specimen in the top bulb. Ideally the lower bulb should contain a small amount of specimen (less than one quarter the volume of the lower bulb).
4. Release the bulb slowly. The transfer pipette barrel should fill completely with some fluid flowing into the smaller (lower) bulb.
5. Place the tip of the transfer pipette into the sample port of the Test Device and squeeze the larger bulb completely. The entire volume of fluid in the transfer pipette barrel must flow into the sample port. The specimen in the smaller (lower) bulb should not be expelled.
   NOTE: Too much specimen has been added to the device if the specimen has migrated outside of the sample port and on to the label.
6. Remove the transfer pipette tip from the sample port and then release the larger (top) bulb.
7. Discard the transfer pipette.
8. Allow specimen to absorb completely before moving the Test Device. At a minimum the sample should be below the sample port opening to be considered fully absorbed.

Step 2 – Run Test
1. From the main screen, select Run Test and press Enter.
2. Select Patient Sample and press Enter.
3. Enter the patient identification number and press Enter.
4. Confirm that the number was entered correctly by selecting Confirm Patient ID and pressing Enter. If the number was not entered correctly, select Correct Patient ID, press Enter and repeat the previous step.
5. Holding the Test Device by the edges, insert the Test Device into the Meter and press Enter. The result will be displayed when the analysis is complete.
   NOTE: The Test Device must be inserted into the Meter within 30 minutes from the time the patient specimen was added. A delay longer than 30 minutes may cause the results to be invalid and blocked out on the printout.

Step 3 – Read the Results
1. Results may be printed by pressing the Print button.
2. Discard the Test Device after release from the Meter.
3. A blocked out result indicates the result was invalid and the test should be repeated.

RESULTS
The Meter measures the target analyte(s) automatically. The results are displayed on the screen. The operator has the option to print the results.
For additional information, refer to the Quidel Triage Meter User Manual.
STANDARDIZATION
The Quidel Triage D-Dimer Test has been standardized using a purified protein preparation of D-dimer based on the mass (concentration) of the analyte present in EDTA anticoagulated plasma.

The D-dimer values are presented in units of mass (ng/mL) of D-dimer, also known as D-dimer Units (D-DU). There are no international standards for D-dimer and different assays use antibodies with differing specificities for D-dimer and other fibrin degradation products. This can lead to poor correlation between methods reporting results in D-DU. Therefore, it is important to establish correlation between methods prior to implementation.

Other D-dimer assays report results in Fibrinogen Equivalent Units (FEU). It is commonly accepted that 1 D-DU = 2 FEU. The lack of standardization and differing antibody configurations reduces the reliability of this conversion factor.

QUALITY CONTROL CONSIDERATIONS
Every Quidel Triage D-Dimer Test Device is a quantitative test that includes two control materials of different concentrations that are run automatically with every patient specimen, external liquid control solution, or proficiency testing sample. If the automatic check of these built-in controls shows that the control value results are within the limits set during manufacturing, the Meter will report a result for the specimen or sample being tested. If the automatic check of these built-in controls shows that the control value results are not within the limits set during manufacturing, a test result will not be reported. Instead, the Meter will display a warning or error message that is described in the Quidel Triage Meter User Manual.

Good Laboratory Practice suggests that external controls should be tested with each new lot or shipment of test materials, every 30 days, and as otherwise required by your laboratory’s standard quality control procedures. Controls should be tested in the same manner as if testing patient specimens. When running patient specimens or external controls, if an analyte fails for any reason (built-in control failure or an external control out of range) no patient results will be reported.

Users should follow government guidelines (for example, federal, state or local) and/or accreditation requirements for quality control.

Performing Quidel Triage System Quality Control - QC Device
Use the QC Device to ensure proper function of the Meter.
Perform QC Device testing for the following conditions:
1. Upon initial setup of the Meter.
2. Each day of patient testing.
3. When the Meter has been transported or moved.
4. Whenever there is uncertainty about the performance of the Meter.
5. Whenever required by your laboratory’s quality control requirements.

Do not discard the Quidel Triage QC Device and associated CODE CHIP module. Store them in the QC Device Box.

Refer to the Quidel Triage User Manual for complete instructions on use of the QC Device.

1. The first time a new QC Device is run in the Quidel Triage Meter, install the QC Device CODE CHIP module. The QC Device CODE CHIP module data is stored in the Meter memory. The QC Device CODE CHIP module does not need to be reinstalled after the first time.

QC DEVICE CODE CHIP MODULE
a. From the main screen, select Install New Code Chip and press Enter.
b. Place the QC Device CODE CHIP module into the lower left front corner of the Meter. Follow the prompts on the screen.
c. Remove the QC Device CODE CHIP module from the Meter when data transfer is complete.
d. Place the QC Device CODE CHIP module back into the QC Device Box for storage.

2. From the main screen, select Run Test and press Enter.
3. If User ID is enabled enter your User ID number and press Enter.
4. Select QC Device and press Enter.
5. Insert QC Device into the Meter and press Enter.
6. A Pass or Fail result will be displayed/printed when complete. Each parameter should pass before patient testing is performed.
7. Remove the QC Device from the Meter and place in the QC Device Box. DO NOT DISCARD THE QC DEVICE.

NOTE: If the QC Device or external controls do not perform as expected, review the above instructions to see if the test was performed correctly, repeat the test, then contact Quidel or your local Quidel representative (refer to the Assistance section). Refer to the Quidel Triage Meter User Manual for a complete description of the quality control system.
LIMITATIONS OF THE PROCEDURE

- The result of the test should be evaluated in the context of all the clinical and laboratory data available. In those instances where the laboratory result does not agree with the clinical evaluation, additional tests should be performed accordingly.
- This test has been evaluated with venous whole blood and plasma using EDTA as the anticoagulant. Other specimen types, draw methods, or anticoagulants have not been evaluated.
- There is the possibility that factors such as technical or procedural errors, as well as additional substances in blood specimens that are not listed below, may interfere with the test and cause erroneous results.
- As with any assay employing mouse antibodies, the possibility exists for interference by human anti-mouse antibodies (HAMA) in the sample. The test has been formulated to minimize this interference; however, specimens from patients who have been routinely exposed to animals or to animal serum products may contain heterophile antibodies which may cause erroneous results.

EXPECTED VALUES - D-DIMER

The expected values were calculated non-parametrically and represent the 95th percentile of the population tested. The expected values from 208 apparently healthy individuals (77 females age 19-79, 131 males age 19-73) are less than 600 ng/mL. The 90th percentile of measurements is less than 400 ng/mL.

Each laboratory should establish a reference range that is representative of the patient population to be evaluated. Additionally, each laboratory should consider the current practice in the evaluation of patients experiencing symptoms at each institution.

PERFORMANCE CHARACTERISTICS

Analytical Sensitivity

The analytical sensitivity or lowest detectable concentration that is distinguishable from zero was determined by testing a zero calibrator 20 times each using 3 lots of reagents and 5 Meters on 3 days. The analytical sensitivity of the Quidel Triage D-Dimer Test is presented below:

<table>
<thead>
<tr>
<th>D-dimer</th>
<th>100 ng/mL</th>
</tr>
</thead>
</table>

Measurable Range

D-dimer: 100 ng/mL to 5,000 ng/mL

Interfering Substances

Hemoglobin (up to 500 mg/dL), lipids (triolein up to 3,000 mg/dL), bilirubin (up to 15 mg/dL), fibrinogen (up to 1 mg/mL), fragment D (up to 20 μg/mL) or fragment E (up to 20 μg/mL) added to EDTA anticoagulated plasma containing D-dimer did not interfere with the recovery of D-dimer.

These substances failed to produce a positive response in a sample that did not contain the analyte of interest. However, severely hemolyzed specimens should be avoided whenever possible. When a sample appears to be severely hemolyzed, another specimen should be obtained and tested.

The hematocrit was varied between 30% and 55% with no significant effect on the recovery of D-dimer. RA factor has not been tested.

Pharmaceuticals

The following drugs were evaluated for potential cross-reactivity and interference in the Quidel Triage D-Dimer Test. All drugs were tested at concentrations that represent the blood concentrations that would result from a maximal therapeutic dose and at least twice the maximal therapeutic dose. There was no significant interference with the analyte, nor was there any assay cross-reactivity.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Cross-reactivity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acebutolol</td>
<td>Cervinatin</td>
</tr>
<tr>
<td>Acetaminophen</td>
<td>Chioramphenicol</td>
</tr>
<tr>
<td>Acetazolamide</td>
<td>Chlorothiazide</td>
</tr>
<tr>
<td>Acetylsalicylic acid</td>
<td>Clofibrate</td>
</tr>
<tr>
<td>Albuterol</td>
<td>Clopidogrel</td>
</tr>
<tr>
<td>Allopurinol</td>
<td>Cocaine</td>
</tr>
<tr>
<td>Amiloride</td>
<td>Cyclosporine</td>
</tr>
<tr>
<td>Amiodarone</td>
<td>Diclofenac</td>
</tr>
<tr>
<td>Amoxicillin</td>
<td>Digoxin</td>
</tr>
<tr>
<td>Ampicillin</td>
<td>Diltiazem</td>
</tr>
<tr>
<td>Ascorbic acid</td>
<td>Dipryridamole</td>
</tr>
<tr>
<td>Atenolol</td>
<td>Dopamine</td>
</tr>
<tr>
<td>Atenosartan</td>
<td>Epropranolol</td>
</tr>
<tr>
<td>Bepridil</td>
<td>Erythromycin</td>
</tr>
<tr>
<td>Caffeine</td>
<td>Fluoxetine</td>
</tr>
<tr>
<td>Captopril</td>
<td>Fosinopril</td>
</tr>
</tbody>
</table>

Imprecision

Within-day and total imprecision were determined using the ANOVA model by testing control materials and human plasma pools that had the respective analytes added at concentrations near the decision points of the assay and throughout the range of the standard curve. The study was conducted over 10 days, testing each control 10 times per day.

D-Dimer:

<table>
<thead>
<tr>
<th>Within Day Imprecision</th>
<th>Mean (ng/mL)</th>
<th>SD (ng/mL)</th>
<th>CV</th>
</tr>
</thead>
<tbody>
<tr>
<td>128</td>
<td>18</td>
<td>14.4%</td>
<td></td>
</tr>
<tr>
<td>451</td>
<td>44</td>
<td>9.7%</td>
<td></td>
</tr>
<tr>
<td>2,990</td>
<td>180</td>
<td>6.0%</td>
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</table>

D-Dimer:

<table>
<thead>
<tr>
<th>Total Imprecision</th>
<th>Mean (ng/mL)</th>
<th>SD (ng/mL)</th>
<th>CV</th>
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<tbody>
<tr>
<td>128</td>
<td>20</td>
<td>15.4%</td>
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<tr>
<td>451</td>
<td>48</td>
<td>10.7%</td>
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</tr>
<tr>
<td>2,990</td>
<td>183</td>
<td>6.1%</td>
<td></td>
</tr>
</tbody>
</table>
Method Comparison - D-dimer

The method comparison was performed using samples from apparently healthy individuals (N = 111, range < 100 ng/mL to 1,850 ng/mL), patients with confirmed pulmonary embolism (N = 17, range 560 ng/mL to > 1,850 ng/mL), patients with myocardial infarction (N = 32, range < 100 ng/mL to 2,630 ng/mL), patients with unstable angina (N = 11, range < 100 ng/mL to 2,910 ng/mL), patients with CHF (N = 4, range 380 ng/mL to 530 ng/mL), and patients with non-cardiac chest pain (N = 5, range < 100 ng/mL to 690 ng/mL). No samples from patients with deep venous thrombosis were included in the study.

A comparison of 180 D-dimer measurements on the Quidel Triage D-Dimer Test to the Stratus CS Acute Care Diagnostic System® D-dimer method yielded the following statistics (Passing-Bablok regression):

<table>
<thead>
<tr>
<th>Slope</th>
<th>Intercept</th>
<th>Correlation coefficient</th>
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<tbody>
<tr>
<td>0.999</td>
<td>-85.89</td>
<td>0.92</td>
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**Altman-Bland Bias Plot**

The Limited Warranty above shall not apply if the Customer has subjected the Product to physical abuse, misuse, abnormal use, use inconsistent with the Product Manual or Insert, fraud, tampering, unusual physical stress, negligence or accidents. Any warranty claim by Customer pursuant to the Limited Warranty shall be made in writing within the applicable Limited Warranty period.

**ASSISTANCE**

If you have any questions regarding the use of this product, please contact Quidel Technical Support at 1.800.874.1517 (in the U.S.) or technicalsupport@quidel.com. If outside the U.S., contact your local distributor or one of the Technical Support Centers listed below. You may also contact us at quidel.com.

<table>
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<th>Region</th>
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<td>+44 161.483.9032</td>
<td><a href="mailto:EMEproductsupport@alere.com">EMEproductsupport@alere.com</a></td>
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<tr>
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BIBLIOGRAPHY OF SUGGESTED READING


