INTENDED USE
ichroma™ D-Dimer along with the ichroma™ Reader is a fluorescence immunoassay that quantifies the total D-Dimer concentration in plasma. The test is used as an aid in the post therapeutic evaluation of thromboembolic disease patients.

INTRODUCTION
D-dimer, a degradation product of cross-linked fibrin formed during activation of the coagulation system, is commonly used to exclude thromboembolic disease in outpatients suspected of having deep venous thrombosis (DVT) and pulmonary embolism (PE).[1] DVT and PE is relatively common and can cause sudden, fatal embolic events in the pulmonary arteries and other regions. [2-3]

Measurement of the D-Dimer level in plasma has been used as a screening strategy for subclinical DVT. A systematic review reported that a normal range of a highly sensitive D-Dimer level accurately ruled out DVT in patients classified as having a low or moderate clinical probability of DVT. The DVT is a high-risk factor for the stroke because of advanced age, hemiplegia, and coagulation disorders, and DVT can cause paradoxical embolic stroke via a right-to-left shunt. Thus, it is important to monitor the level of D-Dimer the incidence and characteristics of DVT in acute stroke patients.[4-7] The Plasma D-dimer level has proven to be useful for DVT screening in chronic stroke patients undergoing rehabilitation.[8-10] National and international scientific organizations have suggested the use of these markers when implementing new diagnostic strategies in patients with coronary syndrome. Since D-Dimer is well known to be an important prognostic indicator of heart diseases, its most definitive role is on monitoring post-treatment clinical status and the post therapeutic evaluation of patients.

ichroma™ D-Dimer Test measures quantitative D-Dimer concentration in human plasma.

PRINCIPLE
The test uses the sandwich immunodetection method, such that the detection antibody in buffer binds to D-Dimer in the plasma sample and antigen-antibody complexes are captured by antibodies that have been immobilized on the test strip as sample mixture migrates through nitrocellulose matrix. The more D-Dimer antigen in the plasma, the more antigen-antibody complexes are accumulated on test strip. Signal intensity of fluorescence on detection antibody reflects amount of antigen captured and is processed by ichroma™ Reader to show D-Dimer concentration in the specimen. The working range of ichroma™ D-Dimer test is 50 – 10,000 ng/ml.

* Reference Value: 500 ng/mL (FEU: Fibrinogen equivalent units)

COMPONENTS AND REAGENTS
ichroma™ D-Dimer consists of Cartridge, an ID Chip, and Detection Buffers.

- The test cartridge contains a test strip; on the membrane of which, antibodies against D-Dimer and streptavidin have been immobilized at the test line and the control line respectively.
- Each test cartridge is individually sealed in an aluminum foil pouch containing a desiccant. 25 sealed test cartridges are packed in a box which also contains an ID chip.
- The detection buffer pre-dispensed in a tube contains fluorochrome-labeled anti-D-Dimer antibodies, fluorescent-labeled biotin-BSA, bovine serum albumin (BSA) as a stabilizer and sodium azide in phosphate buffered saline (PBS) as a preservative.
- The detection buffer is dispensed in each detection buffer tube. 25 detection buffer tubes are packed in a separate pouch which is further packed in a Styrofoam box provided with ice packs for the purpose of shipment.

WARNINGS AND PRECAUTIONS
- For in vitro diagnostic use only.
- Carefully follow the instructions and procedures described in this insert.
- Lot numbers of all the test components (test cartridge, ID chip and detection buffer) must match with each other.
- Do not interchange the test components from different lots or use the test components beyond the expiration date.
- Test performed by using any test component with mismatching lot number or that beyond the expiration date may yield misleading test result(s).
- The test cartridge should remain sealed in its original pouch until use. Do not use the test cartridge that is damaged or already opened.
- Allow a minimum of 30 minutes for the test cartridge to attain room temperature, which has been stored in a refrigerator.
- The detection buffer should attain room temperature prior to performing the test.
- ichroma™ D-Diemi as well as the ichroma™ Reader should be used away from vibration and /or magnetic field. During normal usage, ichroma™ Reader may produce minor vibrations which should be regarded as normal.
- A detection buffer tube should be used for processing one sample only. Similarly a test cartridge should be used for testing one processed sample only. Both the detection buffer...
tube as well as the test cartridge should be discarded after single use.
- Used detection buffer tubes, pipette tips, and test cartridges should be handled carefully and disposed of by an appropriate method in accordance with relevant local regulations.
- An exposure to larger quantities of sodium azide may cause certain health issues like convulsions, low blood pressure and heart rate, loss of consciousness, lung injury and respiratory failure.

STORAGE AND STABILITY
- The test cartridge is stable for 20 months (while sealed in an aluminum foil pouch) if stored at 4 - 30°C.
- The detection buffer dispensed in a tube is stable for 20 months if stored at 2 - 8°C.
- After the test cartridge pouch is opened, the test should be performed immediately.

LIMITATIONS OF THE TEST SYSTEM
ichroma™ D-Dimer provides accurate and reliable results subject to the following constraints:
- Use ichroma™ D-Dimer should be used only in conjunction with ichroma™ Reader.
- The test should always be performed on freshly collected sample(s).
- The test sample must be at room temperature prior to testing.
  - If the test samples are to be shipped for the purpose of this test, appropriate precautions must be exercised.
- Effectiveness of the test is highly dependent on storage of test components and test samples at prescribed optimal conditions.
- The test may yield false positive result(s) due to cross-reactions of some components of serum with the capture/detector antibodies and/or non-specific adhesion of certain components having similar epitopes to bind with these antibodies.
- The test may also yield false negative results; the most common factor being non-responsiveness of the antigen to the antibodies due to its epitopes being masked by some unknown components such that the antigen cannot be detected or captured by the antibodies. False negative results may also be obtained due to instability or degradation of the D-Dimer antigen with time and/or temperature making it unrecognizable by the antibodies.
- Other factors interfering with the test and causing erroneous results include technical/procedural errors, degradation of the test components/reagents as well as presence of interfering substances in the test samples.
- Any clinical diagnosis based on the test result must be supported by a comprehensive judgment of the concerned physician including clinical symptoms and other relevant test results.

SAMPLE COLLECTION AND PREPARATION
The test can be performed with plasma.
- It is recommended to test the sample within 24 hours after collection.
- The serum and plasma should be prepared by centrifugation within 3 hours after the collection of whole blood.
- Take precautions on the handling and storage of sample blood because it's analyzed the concentration of D-Dimer is sensitive to anticoagulant and storage conditions.
- Preparing the Plasma specimen: Collect the blood in a tube treated with sodium citrate.
- Be careful not to have blood sample hemolyzed in the course of handling and centrifugal process.
- Do not keep the sample in a freezer, which could affect the test value of D-Dimer.
- It is recommended to avoid using severely hemolyzed and hyperlipidemia specimens whenever possible. If the specimen appears to be severely hemolyzed, another specimen should be obtained and tested.

MATERIALS PROVIDED
- Box containing Detection Buffer Tube
  - Detection Buffer Tubes 25
- ID Chip 1
- Package Insert 1
- Sealed Test Cartridges 25

MATERIALS REQUIRED BUT NOT PROVIDED
Following items can be purchased separately from ichroma™ D-Dimer. Please contact our sales division for more information.
- ichroma™ Reader FR203
- Thermal Printer

TEST SETUP
1. Check the contents of ichroma™ D-Dimer: Sealed Test Cartridge, ID Chip, and Detection Buffer Tube.
2. Ensure that the lot number of the test cartridge matches with that of the ID chip as well as the detection buffer tube.
3. Keep the sealed test cartridge (if stored in refrigerator) and the detection buffer tube at room temperature for at least 30
minutes just prior to the test. Place the test cartridge on a clean, dust-free and flat surface.
4. Turn on the power supply of the ichroma™ Reader.
5. Insert the ID Chip into the ID chip port of the ichroma™ Reader.
6. Press the ‘Select’ button on the ichroma™ Reader. (Please refer to the ‘ichroma™ Reader Operation Manual’ for complete information and operating instructions.)

**TEST PROCEDURE**
1. Transfer 10 µL of serum/plasma/control sample using a transfer pipette to a tube containing the detection buffer.
2. Close the lid of the detection buffer tube and mix the sample thoroughly by shaking it about 10 times. (The sample mixture must be used immediately.)
3. Pipette out 75 µL of a sample mixture and dispense it into the sample well on the test cartridge.
4. Leave the sample-loaded test cartridge at room temperature for 12 minutes.
5. For scanning, insert it into the test cartridge holder of the ichroma™ Reader. Ensure proper orientation of the test cartridge before pushing it all the way inside the test cartridge holder. An arrow has been marked on the test cartridge especially for this purpose.
6. Press ‘Select’ button on the ichroma™ Reader to start the scanning process.
7. ichroma™ Reader will start scanning the sample-loaded test cartridge immediately.
8. Read the test result on the display screen of the ichroma™ Reader.

**INTERPRETATION OF TEST RESULT**
- ichroma™ Reader calculates the test result automatically and displays D-Dimer concentration of the test sample as ng/mL.
- Working range of ichroma™ D-Dimer is 50-10,000 ng/mL.
- Reference value of ichroma™ D-Dimer is 500 ng/mL. (FEU: Fibrinogen equivalent units)

**Quality Control**
- Quality control tests are a part of the good testing practice to confirm the expected results and validity of the assay and should be performed at regular intervals.
- Before testing a clinical sample using a new test lot, control reagents should be tested to confirm the test procedure, and to verify whether the test produces the expected results.
- Quality control tests should also be performed whenever there is any question concerning the validity of the test results.
- Control reagents are not provided with ichroma™ D-Dimer. For more information regarding obtaining the control reagents, contact Boditech Med Inc.’s Technical Services for assistance.

**ichroma™ D-Dimer test has a built-in internal control that satisfies the routine quality control requirements. This internal control test is performed automatically each time a clinical sample is tested. An invalid result from the internal control leads to display an error message on the ichroma™ Reader indicating that the test should be repeated.**

**PERFORMANCE CHARACTERISTIC**

1. **Specificity**
Other bio-molecules, such as Hb, CEA, AFP, ALP, CRP, Troponin I, CK-MB, Myoglobin, Albumin and specially hyperlipid were added to test specimen with much higher level than their physiological level in normal blood. There was no significant interference with the D-Dimer measurement, nor was their any significant assay cross-reactivity with those bio-molecules.

2. **Imprecision**: For studying intra-assay imprecision, 10 replicates of each of the eight concentrations of spiked plasma samples with Bio-Rad D-Dimer control were tested. For studying inter-assay imprecision, 10 replicates of each of the eight concentrations of spiked plasma samples with Bio-Rad D-Dimer control were tested by four different persons.

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<th>Conc. [ng/mL]</th>
<th>Intra Assay</th>
<th>Inter Assay</th>
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3. **Comparability**
Total D-Dimer concentrations of 100 plasma samples were quantified independently with ichroma™ D-Dimer device and bioMerieux VIDAS automatic analyzer according to established standard test procedure. Test result was compared and their compatibility was investigated with linear regression and correlation of coefficient (R). Linear regression and correlation of coefficient were $Y=0.955X + 47.13$ and $R=0.965$, respectively.
REFERENCES


4. Comparison of an immuno-turbidometric method (STalia R D-

5. Different cut-off values of quantitative D-dimer methods to predict the risk of venous thromboembolism recurrence: a post-hoc analysis of the PROLONG study haematologica | 2008; 93(6) | 901


10. VIDAS#{174}D-dimer: fast quantitative ELISA for measuring D-dimer in plasma JEAN-LOUIS PITTET,† PHILIPPE DE MOERLOOSE,5 GuilDo REBER,5 CATHERINE DURAND,1 CECILE VILLARD,2 NADIA PIGA,2 DOMINIQUE ROLLAND,3 SERGE COMBY,4 and GEORGES Dupuy1 Clinical Chemistry 42, No. 3, 1996

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