ENGLISH

lumiraDx™ D-Dimer Test

For Professional Use Only
SPEC-31057 Rev2
ART-00228 Rev4

LumiraDx D-Dimer Test

The LumiraDx D-Dimer Test Strips (hereafter referred to as Test Strips) are to be used with the LumiraDx Platform. The LumiraDx Platform is a point of care system for professional use which is used for *in vitro* diagnostic tests. It comprises a portable LumiraDx Instrument and a LumiraDx Test Strip for the required test. This test is for **HEALTHCARE PROFESSIONAL USE ONLY** and allows users to perform tests using small sample volumes and to view results quickly on the Instrument touch-screen.

Intended use

The LumiraDx POC D-Dimer Test is an *in vitro* diagnostic test for the quantitative determination of D-dimer in human whole blood (capillary finger stick and venous) and plasma specimens. The test can be used as an aid in the assessment and diagnosis of patients with suspected venous thromboembolism (VTE) such as deep vein thrombosis (DVT) and pulmonary embolism (PE).

Caution: For *in vitro* diagnostic use.

Before you start testing, if you are new to the LumiraDx Instrument and LumiraDx Platform, you must read the LumiraDx Platform User Manual, the LumiraDx D-Dimer Quality Control Pack Insert, and this entire Product Insert. In addition, please watch the LumiraDx Platform Training Video available at lumiradx.com.

Summary and explanation of the Test:

D-Dimer testing is used as an aid in the diagnosis of venous thromboembolism (VTE) and is widely accepted as the first-step in the management of patients with suspected VTE[1].

D-Dimer is a degradation product of fibrin, present in the blood after a blood clot is degraded by fibrinolysis. D-Dimer testing is of clinical use when there is a suspicion of VTE and is used alongside clinical scoring systems and additional test methods.

Principle of the assay:

The LumiraDx D-Dimer Test is a single use fluorescence immunoassay device designed to determine the concentration of D-Dimer in human whole blood (capillary finger stick and sodium citrated-venous) and sodium citrated-plasma specimens.

The test procedure involves the addition of fingerstick, venous whole blood or plasma sample to the sample application area of the Test Strip inserted in the Instrument.

The Test Strip is inserted into the Instrument which is programmed to perform the analysis when the sample has reacted with the reagents within the Test Strip. The analysis is based on the amount of fluorescence the Instrument detects within the measurement area of the Test Strip. The concentration of the analyte in the sample is proportional to the fluorescence detected. The results are displayed on the Instrument touch-screen in approximately 6 minutes from the addition of sample.

Carton contents:

- Test Strips packed separately in desiccant foil pouches
- Product Insert
- RFID (Radio frequency ID) Tag held inside the Test Strip carton.
- Quality Control Ranges Product Insert

Materials required but not provided with the Test Strip carton:

- LumiraDx Instrument
- LumiraDx D-Dimer Quality Controls (as required to meet local and organizational compliance)
- Standard blood collection equipment (high flow lancets, venepuncture, transfer tubes, biowaste disposal)
- LumiraDx Connect if connectivity required (refer to LumiraDx Connect User Manual)
- More information available at lumiradx.com

Reagents: warnings and precautions

- Proper laboratory safety techniques should be followed at all times when working with patient samples. Patient specimens, used Test Strips 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.
- Reagents encapsulated within the Test Strip, are present in extremely small amounts and, where any component is of animal origin, the source is certified as free from infectious or contagious material – however, should any reagent become exposed it should be treated as potentially infectious.

Storing the Test Strips:

Store the Test Strips in their original carton. You can store the Test Strips at a temperature between 2°C and 30°C (36°F and 86°F). Avoid freezing or storing in any area that could exceed 30°C. When stored properly, the Test Strips can be used until the expiration date printed on the Test Strip foil pouch and the Test Strip carton. Discard the Test Strips if they are past the expiration date.

Handling the Test Strips:

When you are ready to perform a test, open the Test Strip carton, take out 1 Test Strip, and remove it from the foil pouch. After removing the Test Strip from the foil pouch, it should be used immediately. Do not use the Test Strip if there are any visible signs of damage to the foil pouch such as tears or holes.

Sample material:

The following samples can be used with the LumiraDx D-Dimer Test Strip:

- Whole blood - Capillary fingerstick sample (direct – non-anticoagulated) or using
- Transfer tube – (Lithium-Heparin anticoagulated)
- Anticoagulated venous whole blood (citrated)
- Plasma (citrated)
- LumiraDx D-Dimer Quality Controls

The Test device contains:

- Mouse monoclonal antibodies
- Fluorescent Latex particles
- Magnetic particles
- Buffer and Stabilising Agents

Specimen sample collection and preparation for analysis:

When collecting any type of sample, follow universal blood collection precautions and guidelines according to your organization. For specimen collection of venous whole blood or plasma, follow the sample tube manufacturer´s recommended procedure.

The steps that follow apply to collecting a capillary blood sample from a finger stick. Optionally, you may use a Transfer Tube to collect the fingerstick blood sample. The Transfer Tube **must** be a Lithium Heparin anticoagulated tube. Details of recommended Transfer Tubes are available at lumiradx.com. Only auto-disabling, single use, high flow lancing devices may be used to collect capillary blood.

When testing from venous whole blood or plasma specimen collect blood by clean venipuncture in trisodium citrate (0.109 mol/L/3.2%), observing the correct anticoagulant to blood ratio.

If using venous whole blood, test patient specimen within 1 hour of sample collection. Whole blood should be processed to plasma within 1 hour of being drawn from the patient. If not testing plasma immediately, it should be stored and transported in a frozen state. No more than a single freeze/thaw cycle is recommended.

Procedure/Performing a Test:

Refer to the LumiraDx Platform User Manual for instructions on how to analyse a patient or Quality Control sample. The LumiraDx Platform Quick Reference Guide also provides an illustrated step by step procedure. Before running a LumiraDx D-Dimer Test you must transfer the LumiraDx Lot Calibration File into the Instrument from the RFID Tag in the Test Strip Carton. This is explained in the LumiraDx Platform User Manual. When indicated by the touch-screen, open the foil pouch just before use and insert the LumiraDx Test Strip into the LumiraDx Instrument. The Instrument will indicate when ready for the sample to be applied.

The LumiraDx D-Dimer Test results should be evaluated in the context of all the clinical and laboratory data available by a Healthcare Professional. In those instances where the laboratory result does not agree with the clinical evaluation, additional tests should be performed accordingly.

Testing from a fresh capillary fingerstick sample

1. **Collecting a capillary blood sample from a finger stick:** Ensure the patient thoroughly washes and dries their hands with warm soapy water prior to sample collection. **Note:** the hands must be completely clean of all hand oils, lotions, gels, sanitizers and/or any foreign matter prior to sample collection, which may otherwise cause unreliable results. If isopropyl alcohol (IPA) wipes are used, wipe the finger stick site with a gauze pad and make sure the site is completely dry. If any alcohol remains (or is reintroduced) on the finger, it may cause unreliable results. Increasing the blood flow in the finger will help to get a good drop of blood. Before lancing the finger, the following techniques can be used until the fingertip has increased colour:
   - Ask the patient to rinse their hands with warm water.
   - Ask the patient to hold his or her arm straight down at their side
   - Massage the finger from its base, and if required, immediately after lancing, very gently squeeze the finger from its base to encourage blood flow.
2. **Use a high flow lancet** on the selected finger to obtain a blood sample.
3. **Immediately apply the sample** by holding the finger and the hanging blood drop over the Sample Application Area of the inserted Test Strip. Allow the blood drop to touch the Sample Application Area of the Test Strip. Blood will then be drawn by capillary action into the Test Strip. When the sample is detected the Instrument will sound (if sounds are enabled) and a confirmation message will be displayed. The touch-screen of the LumiraDx Instrument will request the user to close the door.
4. **Do not add more blood**. Do not open the door while the test is in progress. The touch-screen will indicate test progress.
5. **The result** will appear on the Instrument touch-screen within approximately 6 minutes of applying the sample and starting the test.
6. **Dispose** of the lancet and Test Strip in the appropriate clinical waste.
7. **Clean** the patient's finger with a clean tissue and apply slight pressure.
8. If you need to retest, use a new Test Strip and lancet, and a different finger.
9. **Disinfection** of the Instrument with LumiraDx approved materials is recommended after each patient sample or if contamination is suspected. Details of approved disinfecting materials are available at lumiradx.com. Allow the Instrument to air dry before testing the next sample. The disinfectant should remain in contact for at least 5 minutes.

Using a Transfer Tube from a capillary finger stick sample

You **must** use a Lithium Heparin anticoagulated Transfer Tube to transfer the capillary sample from the finger stick to the Sample Application Area of the Test Strip. To do this, follow the procedure above for collecting a capillary blood sample from a finger stick. Use the Transfer Tube by placing it into the blood droplet on the finger, and the blood should quickly move into the tube. Then hold the Transfer Tube over the Sample Application Area of the Test Strip and dispense the sample. This should be enough just to fill the Sample Application Area. Take care not to introduce air bubbles into the sample. When the sample is detected the Instrument will sound (if sounds are enabled) and a confirmation message will be displayed. The touch-screen of the LumiraDx Instrument will request the user to close the door. Dispose of the Transfer Tube in the appropriate clinical waste. Follow instructions from step 4.

Testing from venous blood and plasma sample

Mix the sample well before testing. You may use venous blood or plasma samples for testing. Use a pipette to remove 20µl of sample from the tube. Hold the pipette over the Sample Application Area of the Test Strip and dispense the sample. This should be enough just to fill the Sample Application Area. Take care not to introduce air bubbles into the sample. When the sample is detected the Instrument will sound (if sounds are enabled) and a confirmation message will be displayed. The touch-screen of the LumiraDx Instrument will request the user to close the door. Follow instructions step 4 and 5.

Sample application using a transfer tube

Sample covering Sample Application Area

Testing patient specimens procedural notes:

Refrigerated whole blood or plasma specimens must be allowed to reach room temperature and be mixed thoroughly before testing.

- Before use, mix whole blood venous specimens by gently inverting the tube several times.
- Before use, mix plasma specimens by vortexing or inverting the tube several times.

Built-in controls:

The LumiraDx Instrument and LumiraDx D-Dimer Test Strips have several quality control functions integrated to ensure validity of each test run. These checks ensure that the behaviour of the sample moving into the reaction area of the Test Strip is as expected. The checks also ensure that the Test Strip has not been previously used and that whole blood samples outside the accepted hematocrit range are identified. When these checks are not successful, the test run will be rejected and an error message presented on the Instrument touch-screen. For more information about the built-in quality control functions, see the LumiraDx Platform User Manual.

Hematocrit (Hct) range:

The Hct level is determined by the Instrument for each blood sample applied to the test. The LumiraDx D-Dimer Test can be used with blood samples with Hct levels of 25-55% Hct. Samples with Hct levels outside this range are shown as 'Hct Out of Range' on the Instrument touch-screen. No D-Dimer value is reported in samples with Hct 'Out of Range'.

Quality controls:

Liquid Quality Controls are available from LumiraDx (lumiradx.com) or at the Customer Services number. Quality Control testing policy is at the discretion of your organization.

To complete Quality Control assessment of the LumiraDx Instrument and D-Dimer Test Strips, you must use the LumiraDx D-Dimer Quality Controls. The Quality Controls come in two Levels. The frequency of testing will be determined by local guidelines. Refer to the LumiraDx D-Dimer Quality Controls pack insert for information on testing procedure for the LumiraDx Quality Controls.

Cleaning and disinfection

It is recommended to disinfect the Instrument after each patient sample, or if contamination is suspected. Excessive liquid may damage the Instrument. It is important for the protection of the Instrument that exposure to excess moisture is prevented. All disinfection cloths and/or wipes should only be slightly damp, with any excess liquid being manually removed from the cloth before use. Alcohol wipes alone are not sufficient to disinfect the Instrument for blood-based samples, due to the potential presence of bloodborne pathogens.

1. Using a LumiraDx recommended disinfecting material, wipe the external surfaces of the Instrument while taking care to avoid the door hinges, Test Strip inlet, power cord, and USB port.
2. Allow the disinfectant at least 5 minutes contact time with the Instrument before testing the next sample.
3. Dispose of disinfectant materials in accordance with local biohazardous waste disposal procedures.

To clean the Instrument wipe the external surfaces with a soft, slightly damp cloth when it appears visibly dirty.

For more information, or for the full procedure on cleaning and disinfection, please refer to the Technical Bulletin Platform Disinfection Procedure at www.lumiradx.com.

Limitations of the procedure:

- The LumiraDx D-Dimer Test uses fresh capillary whole blood, venous blood and plasma samples. The sample size must be a minimum of 15µL in volume. Low sample volume will cause an error message. Never add more blood to the Test Strip after the test has begun.
- Use the Test Strip only once and then dispose of it appropriately in clinical waste.
- 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.
- Blood specimen types, draw methods or anticoagulants different from those described in this product insert have not been evaluated.
- 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 animal serum products may contain heterophile antibodies which may cause erroneous results.
- The Test has been formulated to minimise interference from Rheumatoid Factors (RF), however, due to the heterogeneity of RF specimens from patients with highly elevated RF may cause erroneous results.
- Hematocrit values between 25% and 55% do not significantly affect test results. Hematocrit values outside the range 25-55% will generate an error message showing 'Hct Out of Range' and no D-Dimer result will be reported.
- Any unusual result must always be followed up to identify the potential cause.
- Results that do not match the clinical symptoms should be repeated to rule out a procedural error.
- When performing a new test or repeating a patient test, always use a new lancet to obtain a fresh drop of blood from a different finger and use a new Test Strip.
- Unusual Results: If the LumiraDx Instrument displays an error message, refer to the Troubleshooting section of the LumiraDx Platform User Manual. If the LumiraDx Instrument displays an unexpected test result (other than an error message), check this Limitations section.

Results

Specific performance characteristics

Expected values:

The LumiraDx D-Dimer Test used with the LumiraDx Instrument has a reportable range of 190 - 4000µg/L Fibrinogen Equivalent Units (FEU).

In a study carried out using 127 citrated plasma samples from normal, healthy volunteers (age 18-50 years), 90% of values were below 533 µg/L (FEU).

Each laboratory should investigate the transferability of the expected values to its own patient population and, if necessary, determine its own reference ranges.

Matrix comparison

The matrix comparison was performed using paired: fingerstick capillary (direct), fingerstick capillary (Lithium Heparin Transfer Tube), venous citrated blood and venous citrated plasma samples from 95 patients with D-Dimer concentrations between 55 – 3335 µg/L. All sample types were shown to give the following results when compared with citrated plasma by regression testing.

Correlation between:

- Capillary blood (direct application) and citrated plasma on LumiraDx D-Dimer Test (n = 95): concordance = 91.6%
- Capillary blood (Lithium-Heparin Transfer Tube) and citrated plasma (n = 93): concordance = 91.4%
- Venous citrated blood and citrated plasma (n = 95): concordance = 96.8%

Linearity:

Linearity was established according to a protocol based on CLSI EP06-A[2]. A low and high pool was prepared by pooling clinical, citrated plasma samples. A Linearity series was then prepared by mixing the low and high pools together. The results obtained confirm linearity across the measuring range of 157 to 3593 µg/L.

Detection capability:

Detection Capability studies were performed according to a protocol that was based on the CLSI EP17-A2[3] guideline. The studies were carried out in venous blood and plasma with 1 lot of Test Strips. Limit of blank (LoB) was calculated non-parametrically using 4 samples depleted of D-Dimer, on 10 Instruments over 2 days. Limit of Detection (LoD) was determined non-parametrically using 4 low concentration D-Dimer samples, on 10 Instruments over 2 days. The Limit of Quantitation (LoQ) was determined by testing 5 low concentration D-Dimer samples, on 10 Instruments over 2 days.

Detection Limit	D-Dimer Conc. (µg/L)
LoB	152
LoD	190
LoQ	190

Hook effect:

No hook effect was observed up to a tested concentration of 20,000 µg/L.

Precision:

A precision study was carried out in citrated venous plasma on a protocol based on CLSI EP5-A3[4]. The study was carried out with levels of D-Dimer, each was tested in 2 runs of 2 replicates per day, for twenty days. The results of the precision study are summarised below:

D-Dimer conc (µg/L)	Within run precision (%CV)	Within day precision (%CV)	Between day precision (%CV)	Total precision (%CV)	n
291	9.8	11.1	0.0	11.1	80
552	9.4	9.4	2.5	9.7	80
1790	10.1	10.1	0.7	10.2	80

Fingerstick capillary, citrated venous blood and citrated plasma precision was calculated using the average paired replicate %CV from 98, 90 and 95 patient samples respectively with D-Dimer concentrations between 55 – 3335 µg/L. Calculated % CV for fingerstick capillary, venous whole blood and plasma was 9.5%, 9.0%, and 7.6% respectively.

Method comparison

The method comparison was performed using plasma samples from patients (n=327, range= 60 - 4515µg/L FEU). A comparison of 1767 D-Dimer measurements with the LumiraDx D-Dimer Test to the VIDAS Exclusion II D-Dimer assay yielded the following statistics: Slope = 1.02, Intercept = 21, r = 0.92.

Interference

Testing was performed according to a protocol based on CLSI EP07-ED3[5]. Testing was carried out using whole blood samples at three concentrations of D-Dimer (<500 µg/L, 500 µg/L & 3000 µg/L) spiked with interfering substances. The following interferents showed no significant effect on D-Dimer Test results (<10% difference compared to negative control with 95% confidence).

Exogenous (test concentration)

Acetaminophen (15.6mg/dL), total salicylate – acetylsalicylic acid (3mg/dL), Allopurinol (6mg/dL), Amlodipine (0.0075 mg/dL), Ampicillin (7.5 mg/dL), Apixaban (0.0315 mg/dL), Ascorbic Acid (5.25 mg/dL), Atorvastatin (0.075 mg/dL), Biotin (0.351 mg/dL), Bisoprolol (0.0258 mg/dL), Cholecalciferol (9.6 x 10-4 mg/dL), Cyclosporine A (0.144 mg/dL), Dabigatran (0.9 mg/dL), Doxycycline (1.8 mg/dL), Erythromycin (13.8 mg/dL), Heparin (Sodium) (3300 IU/L), Ibuprofen (21.9 mg/dL), Lidocaine (1.5 mg/dL), L-Thyroxine (0.0429 mg/dL), Metformin (1.2 mg/dL), Omeprazole (0.84mg/dL), Ramipril (0.0156 mg/dL), Salbutamol (0.0045 mg/dL), Trimethoprim (3.36 mg/dL), Warfarin (6 mg/dL).

Endogenous (test concentration)

Bilirubin (unconj) (20 mg/dL), Fibrinogen (600mg/dL), FDP-D (0.036mg/dL), FDP-E (0.714mg/dL), FDP-X (0.2mg/dL), Hemoglobin (via Hemolysis) (815 mg/dL), Lipemia (Triglycerides) (700 mg/dL), Total Protein (1,180 mg/dL).

It is possible that other substances and/or factors not listed above may interfere with the test and cause inaccurate results.

Symbols glossary

Symbol	Meaning
	Temperature limitation
	Manufacturer
IVD	*In vitro* diagnostic medical device
REF	Catalogue number
LOT	Lot number
	Use-by Date – indicates the date after which the unopened IVD/Quality Control material cannot be used
CE	CE Mark *. This product fulfils the requirements of the European Directive 98/79/EC on in vitro diagnostic medical devices.
	Refer to instructions for use.
	Do not re-use
	Indicates the presence of the Radio Frequency Identification (RFID) reader/tag.
EC REP	Authorized Representative in the European Union

References:

1. Rodger MA, Le Gal G, Wells P et al. Clinical decision rules and D-Dimer in venous thromboembolism: current controversies and future research priorities. Throm Res 2014; 134,4: 763-68
2. CLSI EP06-A
3. CLSI EP17-A2
4. CLSI EP5-A3
5. CLSI EP07-ED3

Visit www.CLSI.org for information.

LumiraDx customer services:

For product inquiries please contact LumiraDx Customer Services at customerservices@lumiradx.com or find telephone contact details at lumiradx.com.

Any adverse results experienced with the use of this product, and/or quality problems should also be reported to LumiraDx Customer Services by email: customerservices@lumiradx.com or at lumiradx.com.

For return policy

If there is a problem with the **LumiraDx D-Dimer Tests** you may be asked to return them. Before returning tests please obtain a return authorization number from LumiraDx Customer Services. This return authorization number must be on the shipping carton for return. For ordinary returns following purchase, please contact LumiraDx Customer Services for terms and conditions.

Limited warranty

LumiraDx D-Dimer Test Strips – As per shelf life.

Unused Test Strips must be stored according to the required storage conditions as printed in this product insert and they can be used only up to the expiry date printed on the Test Strip pouch and Test Strip box. For the applicable warranty period, LumiraDx warrants that each product shall be (i) of good quality and free of material defects, (ii) function in accordance with the material specifications referenced in the product insert, and (iii) approved by the proper governmental agency authorized for the sale of products for their intended use (the "limited warranty"). If the product fails to meet the requirements of the limited warranty, then as customer's sole remedy, LumiraDx shall either repair or replace, at LumiraDx's discretion, the Test Strips. Except for the limited warranty stated in this section, LumiraDx disclaims any and all warranties, express or implied, including but not limited to, any warranty of merchantability, fitness for a particular purpose and non-infringement regarding the product. LumiraDx's maximum liability with any customer claim shall not exceed the net product price paid by the customer. Neither party shall be liable to the other party for special, incidental or consequential damages, including, without limitation, loss of business, profits, data or revenue, even if a party receives notice in advance that these kinds of damages might result. The Limited Warranty above shall not apply if the customer has subjected the LumiraDx D-Dimer Test Strips to physical abuse, misuse, abnormal use, use inconsistent with the LumiraDx Platform User Manual or Product Insert, fraud, tampering, unusual physical stress, negligence or accidents. Any warranty claim by Customer pursuant to this Limited Warranty shall be made in writing within the applicable Limited Warranty period.

Intellectual property:

The LumiraDx Instrument, Test Strips and all provided LumiraDx documentation ('Products') are protected by law. The Intellectual Property of the LumiraDx Products remains at LumiraDx. Details of relevant Intellectual Property regarding our products can be found at lumiradx.com/IP Test Strips contained herein include reagents provided under license right from TriLink BioTechnologies LLC.

Legal notices:

Manufacturer information:

LumiraDx UK Ltd, Dumyat Business Park, Alloa, FK10 2PB, UK - Registration number: 09206123

EC REP LumiraDx AB, Västra Vägen 5A, 16961 Solna, Sweden

CE mark applies to LumiraDx Instrument, Test Strips, Quality Controls and Connect Hub only.