ENGLISH

lumiraDx™ D-Dimer

For Professional Use Only

ART-03432 R2 Date of Rev 2024-04

IVD

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IVD

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 D-Dimer test is an *in vitro* diagnostic test for the quantitative determination of D-Dimer in human capillary and venous whole blood and plasma samples (Sodium Citrate). The LumiraDx D-Dimer Test Strips are intended for use with the LumiraDx Instrument. It is an automated *in vitro* diagnostic test for near-patient testing to aid in the assessment and diagnosis of patients with suspected venous thromboembolism (VTE) such as deep vein thrombosis (DVT) and pulmonary embolism (PE).

The test can be used in conjunction with a clinical pre-test probability assessment model to exclude deep vein thrombosis (DVT) and pulmonary embolism (PE) disease in patients suspected of DVT or PE. The LumiraDx D-Dimer test is for Professional Use Only. For patients ≥18 years of age.

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 Quick Reference Instructions, 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 pre-test probability scoring systems and additional test methods such as ultrasound.

D-Dimer levels are almost always increased in cases of VTE. A normal D-Dimer result can exclude patients from the VTE pathway in conjunction with a low-risk clinical pre-test probability score[2]. Please refer to the Expected Values section for more information.

Principle of the assay:

The LumiraDx D-Dimer test is a rapid microfluidic immunofluorescence assay for use with the LumiraDx Instrument for the quantitative measurement 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. 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.

Materials provided:

- LumiraDx D-Dimer Test Strips packed individually in desiccant foil pouches
- LumiraDx D-Dimer Product Insert
- RFID (Radio frequency ID) Tag held inside the Test Strip carton

Materials required but not provided with the Test Strip carton:

- LumiraDx Instrument
- LumiraDx Multi 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)

Warnings and precautions:

- For *in vitro* diagnostic use only
- Do not open the Test Strip until ready for immediate use
- Discard and do not use any damaged or dropped Test Strips or other materials
- Inadequate or inappropriate sample collection, storage, and transport can result in incorrect results
- The test cannot be visually interpreted; the LumiraDx Instrument must be used to generate results
- Do not use the kit components beyond the expiration date
- Do not reuse any kit components
- Samples must be processed as indicated in the Performing a Test section of this Product Insert. Failure to follow the instructions for use can result in inaccurate results
- All components of this kit should be discarded as Biohazard waste according to local regulations and procedures
- Refer to the product safety data sheet for risk and safety phrases and disposal information. The product safety data sheet is available via our website lumiradx.com
- Exercise the normal precautions required for handling all laboratory reagents. Wear protective clothing such as laboratory coats, disposable gloves, and eye protection when samples are collected and evaluated
- Proper laboratory safety techniques should be followed at all times when working with patient samples. Patient samples, used Test Strips and used blood collection equipment may be potentially infectious. Proper handling and disposal methods should be established by the laboratory in accordance with local regulations and procedures.

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 a Test Strip, and remove it from the foil pouch. Hold the Test Strip by gripping the blue label end with the label facing upwards. Do not touch the Test Strip Sample Application Area. Do not bend or fold the Test Strip. Do not touch the Test Strip contacts. 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 – nonanticoagulated) or using Transfer tube – (Lithium-Heparin anticoagulated)
- Anticoagulated venous whole blood (citrated)
- Plasma (citrated)
- LumiraDx Multi Quality Controls

The test device contains:

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

Sample collection and preparation for analysis:

Note: it is recommended to analyse both venous blood and venous plasma immediately after draw.

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, it is recommended to analyse the sample immediately after draw. If not possible to analyse the sample immediately, at a maximum, test the venous whole blood patient specimen within no more than 1 hour of sample collection. Whole blood should be processed to plasma within no more than 1 hour of being drawn from the patient. If not testing plasma immediately, it should be stored frozen at a temperature between -70°C and -80°C (-94°F and -112°F). No more than a single freeze/ thaw cycle is recommended.

Preparing the Instrument to perform a test:

Power on the Instrument by pressing the power button at the rear of the Instrument. You will hear the Instrument powering on, and the display will be a blank black screen for several seconds before starting up. If the screen is just dimmed tap the touch-screen to wake up the Instrument.

Refer to the section on Performing a Test in this Product Insert for information on how to test a Patient sample. The LumiraDx Quick Reference Instructions (QRI) provide an illustrated step-by-step procedure on how to run a Test. Operate the LumiraDx Platform with the D-Dimer test at room temperature between 15°C and 30°C (59°F and 86°F) and 10% - 90% relative humidity.

The Instrument will prompt to install the Lot Calibration File when inserting a new Test Strip Lot. Once installed, the Instrument will have all the information required to process the test, and any future tests from the same Lot of Test Strips.

Lot Calibration File installation

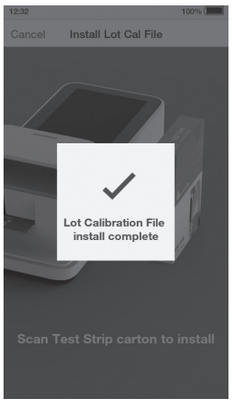
Lot Calibration Files are required to provide the Instrument with the information needed to perform diagnostic tests. This only needs to be completed once for each Test Strip Lot. The Instrument will prompt to install the Lot Calibration File when inserting a new Test Strip Lot.

RFID strip code reader

Locate ((•)) symbol on Instrument.

Installation

Touch back of Test Strip Carton ((•)) symbol to install.



The instrument will sound and a confirmation message will be displayed.

When indicated by the touchscreen, open the foil pouch just before use and insert the LumiraDx Test Strip into the LumiraDx Instrument. The Instrument will indicate when it is ready for the sample to be applied.

The LumiraDx D-Dimer test results should be evaluated by a Healthcare Professional in the context of all available clinical and laboratory data.

Testing from a fresh capillary fingerstick sample:

- **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.

1. **Use a high flow lancet** on the selected finger to obtain a blood sample.
2. **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.
3. **Do not add more blood.** Do not open the door while the test is in progress. The touch-screen will indicate test progress.
4. **The result** will appear on the Instrument touch-screen within approximately 6 minutes of applying the sample and starting the test.
5. **Dispose** of the lancet and Test Strip in the appropriate clinical waste.
6. **Clean** the patient's finger with a clean tissue and apply slight pressure.
7. If you need to retest, use a new Test Strip and lancet, and a different finger.

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.

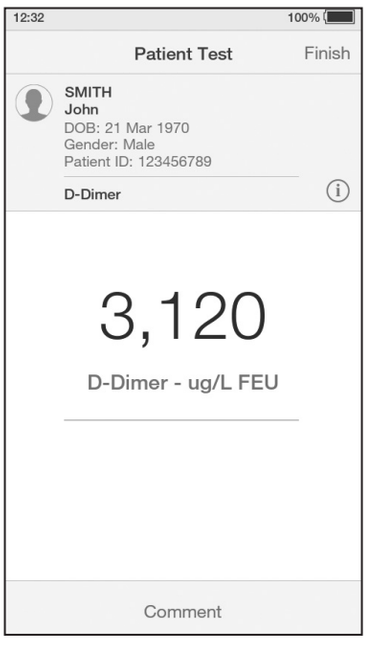
Testing from venous blood and plasma sample:

Note: it is recommended to analyse both venous blood and venous plasma immediately after draw.

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.

Results interpretation:

The results will be displayed on the Instrument screen – The system default unit of measurement is µg/L FEU. Units of measurement are configurable via the Settings Menu. Please refer to the results section for more details – **example of results screen display:**

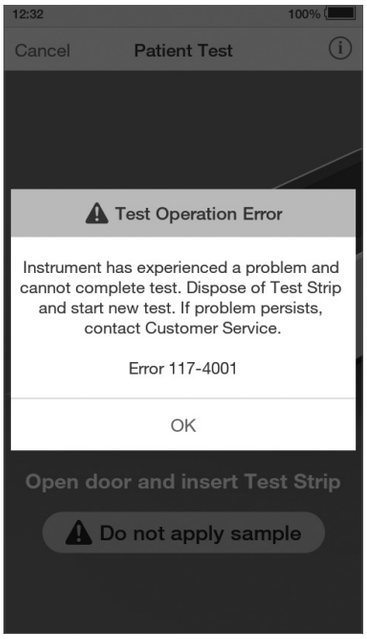


Invalid test results:

If an issue occurs, a message will be displayed on the Instrument touchscreen. Alert messages include useful information and are highlighted by an orange banner. Error messages also include a ⚠ symbol. All messages will contain a description of the Instrument status or error and an instruction. Error messages contain an identifying code that may be used for further troubleshooting purposes. Refer to the LumiraDx Platform User Manual if an error message is displayed on the LumiraDx Instrument touch-screen and contact LumiraDx Customer Services.

Example of an error screen:

If the On Board Control (OBC) fails, an error message will be shown and no test result will be returned. Follow the on screen instructions to dispose of the Test Strip and start a new test. If the problem persists, contact Customer Services.



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 Instrument reads the 2D barcode on each Test Strip and can identify if the Test Strip has exceeded the expiry date for use, and if the Test Strip Lot Calibration file has not yet been loaded at which point it will request it.

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 volume of sample added is sufficient and the assay sequence of the Test Strip is as expected. The checks also ensure that the Test Strip has not been damaged or used previously. If these checks are not verified, the test run will be rejected and an error message displayed on the Instrument touchscreen.

The LumiraDx Instrument ensures the quality of test results obtained through the following features:

- Automated checks of the correct functioning of the Instrument at power on and during operation. This includes electrical component operation, heater operation, battery charge state, mechanical actuators and sensors and optical system performance.
- Monitoring of Test Strip performance and controls during test runtime.
- Ability to perform Quality Control Tests using LumiraDx Quality Control solutions to meet regulatory compliance requirements.

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 20-55% 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".

External Quality Controls:

External liquid Quality Controls for LumiraDx D-Dimer are available from LumiraDx and may be used to demonstrate that the Test is functioning properly by demonstrating the expected Quality Control results and correct test performance by the operator. External Quality Control requirements should be established in accordance with local and organizational compliance. It is recommended that external control testing be performed with each new operator and before using a new lot or shipment of the LumiraDx D-Dimer. Refer to the LumiraDx Multi Quality Controls insert available at lumiradx.com for detailed instructions. LumiraDx Multi Quality Controls are purchased separately.

If the LumiraDx Multi Quality Controls do not perform as expected, repeat the QC Test and if the problems persist, do not report patient results and contact LumiraDx Customer Services.

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 lumiradx.com.

Limitations:

- 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 20% and 55% do not significantly affect test results. Hematocrit values outside the range 20-55% 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.
- The assay has not been validated for individuals younger than 18 years old.
- 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.
- The LumiraDx D-Dimer test is not validated in pregnant women.
- Venous whole blood and venous plasma samples should be tested immediately after initial blood draw. Increased D-Dimer values can be observed if specimen collection and time to analysis recommendations are not followed precisely.
- False negative results can occur in patients who have been recently treated with anticoagulation medications, including patients receiving therapeutic heparin treatment or patients with suspected DVT during oral anticoagulant therapy[3].
- When used for diagnostic purposes, each LumiraDx D-Dimer test result should always be used in conjunction with a clinical pre-test probability score, including but not limited to a full patient examination, their corresponding medical history, and any other relevant clinical information.
- It is not recommended to perform a D-Dimer test on a patient who has a high clinical pre-test probability score.
- It is not recommended to perform a D-Dimer test on patients with symptoms of a VTE for over 14 days[3].

Results:

The LumiraDx D-Dimer test measures D-Dimer concentration via measurement of an optical signal generated when the fluorescent immunoassay (FIA) reagents deposited on the Test Strip are resuspended in the patient sample. The measured optical signal is proportional to the D-Dimer concentration. The optical signal is then converted to D-Dimer concentration via use of a calibration curve, which is established per lot of Test Strips during the calibration process.

Each D-Dimer result is reported on screen with a minimum of 1 and a maximum of 4 of the following user-selectable units:

1. µg/L fibrinogen equivalent units (FEU)
2. mg/L fibrinogen equivalent units (FEU)
3. ng/mL fibrinogen equivalent units (FEU)
4. µg/mL fibrinogen equivalent units (FEU)

The system default unit of measurement is µg/L FEU. Units of measurement are configurable via the Settings Menu. Please refer to the Platform User Manual for more information.

The below table details the conversions between each unit of measurement:

µg/L FEU	mg/L FEU	ng/mL FEU	µg/mL FEU
1	0.001	1	0.001

Performance characteristics:

Expected values:

The LumiraDx D-Dimer test used with the LumiraDx Instrument has a reportable range of:

190 – 4000 µg/L FEU, (0.19 – 4 mg/L FEU), (190 – 4000 ng/mL FEU), (0.19 – 4 µg/mL FEU).

LumiraDx D-Dimer Result	Recommended Outcome
<500 µg/L FEU <0.5 mg/L FEU <500 ng/mL FEU <0.5 µg/mL FEU	If clinical pre-test probability scores are low, VTE is considered to be unlikely.
≥500 µg/L FEU ≥0.5 mg/L FEU ≥500 ng/mL FEU ≥0.5 µg/mL FEU	VTE cannot be excluded as a potential clinical outcome. Follow local guidelines and clinical pathways to further investigate.

Refer to the Clinical Performance section of this Product Insert for more information.

Please note that the above does not take into account age adjusted D-Dimer values.

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 FEU, (0.055 – 3.335 mg/L FEU), (55 – 3335 ng/mL FEU), (0.055 – 3.335 µg/mL FEU)

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-A4. 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 FEU, (0.157 to 3.593 mg/L FEU), (157 to 3593 ng/mL FEU), (0.157 to 3.593 µg/mL FEU)

Detection capability:

Detection Capability studies were performed according to a protocol that was based on the CLSI EP17-A2[5] 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 FEU	mg/L FEU	ng/mL FEU	µg/mL FEU
LoB	152	0.152	152	0.152
LoD	190	0.19	190	0.19
LoQ	190	0.19	190	0.19

Hook effect:

No hook effect was observed up to a tested concentration of 20,000 µg/L FEU, (20 mg/L FEU), (20,000 ng/mL FEU), (20 µg/mL FEU).

Precision:

A precision study was carried out in citrated venous plasma on a protocol based on CLSI EP5-A3[6]. 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	Within run precision (%CV)	Within day precision (%CV)	Between day precision (%CV)	Total precision (%CV)	n
291 µg/L FEU 0.291 mg/L FEU 291 ng/mL FEU 0.291 µg/mL FEU	9.8	11.1	0.0	11.1	80
552 µg/L FEU 0.552 mg/L FEU 552 ng/mL FEU 0.552 µg/mL FEU	9.4	9.4	2.5	9.7	80
1790 µg/L FEU 1.79 mg/L FEU 1790 ng/mL FEU 1.79 µg/mL FEU	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 FEU, (0.055 – 3.335 mg/L FEU), (55 – 3335 ng/mL FEU), (0.055 – 3.335 µg/mL FEU).

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 - 4515 µg/L FEU, (0.06 – 4.515 mg/L FEU), (60 – 4515 ng/mL FEU), (0.06 – 4.515 µg/mL 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.

Clinical performance:

Using LumiraDx D-Dimer test in conjunction with a patient's pre-test probability (PTP) to exclude venous thromboembolism (VTE) - prospective study.

A prospective clinical study was performed on 585 subjects where fresh samples (capillary blood, venous (blood citrated) and plasma (citrated)) were collected from patients presenting with symptoms of VTE (PE or DVT)[8,9]. Subjects also required an assessment with the Wells score and were classed as PTP "Likely" or PTP "Unlikely". The overall prevalence of VTE within this study population was 9.1%. Those with 'Unlikely' PTP categorization were further analysed using the LumiraDx D-Dimer test with a D-Dimer cut-off of 500 µg/L FEU, (0.5 mg/L FEU), (500 ng/mL FEU), (0.5 µg/mL FEU). The sensitivity, specificity, positive and negative predictive values (PPV, NPV) are summarised below with corresponding Wilson Score 95% confidence intervals (CI).

Estimate	Matrix	Patients with Suspected VTE
		Unlikely PTP
Sensitivity % (95% CI)	Venous	100.0% (74.1%-100.0%; n = 378)
	Capillary Direct	100.0% (72.2%-100.0%; n = 377)
	Plasma	100.0% (74.1%-100.0%; n = 406)
NPV % (95% CI)	Venous	100.0% (98.3%-100.0%; n = 378)
	Capillary Direct	100.0% (98.1%-100.0%; n = 377)
	Plasma	100.0% (98.1%-100.0%; n = 406)
Specificity % (95% CI)	Venous	60.2% (55.1%-65.1%; n = 378)
	Capillary Direct	55.3% (50.2%-60.3%; n = 377)
	Plasma	51.1% (46.2.%-56.0%; n = 406)
PPV % (95% CI)	Venous	7.0% (4.0%-12.1%; n = 378)
	Capillary Direct	5.7% (3.2%-10.3%; n = 377)
	Plasma	5.4% (3.0%-9.4%; n = 406)

Clinical Performance using LumiraDx D-Dimer test in conjunction with a patient's pre-test probability to exclude Pulmonary Embolism (PE) – retrospective plasma study.

A study was performed using frozen characterized samples from patients from a prospective clinical study of patients presenting with symptoms of PE. Pre-test probability (PTP) assessment was performed using the simplified, revised Geneva score, resulting in high, intermediate, and low PTP10. The population contained 549 patients with low or intermediate PTP. The prevalence of PE in this group was 15.1% (83/549). The sensitivity (PPA), specificity (NPA), positive and negative predictive values (PPV, NPV) with corresponding 95% Wilson score confidence intervals (CI) for the clinical performance of the LumiraDx D-Dimer Test in this study population are summarized below with using a D-Dimer cut off of 500 µg/L FEU, (0.5 mg/L FEU), (500 ng/mL FEU), (0.5 µg/mL FEU).

Estimate	Patients with suspected PE
	low + intermediate PTP (n=549)
Sensitivity % (95% CI)	100.0% (95.6%-100.0%)
NPV % (95% CI)	100.0% (98.1%-100.0%)
Specificity % (95% CI)	42.1% (37.7%-46.6%)
PPV % (95% CI)	23.5% (19.4%-28.2%)

Interference

Testing was performed according to a protocol based on CLSI EP07-ED3[7]. Testing was carried out using whole blood samples at three concentrations of D-Dimer spiked with interfering substances.

µg/L FEU	mg/L FEU	ng/mL FEU	µg/mL FEU
<500	<0.5	<500	<0.5
500	0.5	500	0.5
3000	3	3000	3

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 (9.6×10^{-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
	*In vitro* diagnostic medical device
	Catalogue Number
	Lot Number
	Use-by Date – indicates the date after which the unopened IVD/Quality Control Material cannot be used
	Refer to instructions for use
	Do not re-use
	For near patient testing
	"CE Mark ". This product fulfils the requirements of the European Directive 98/79/EC on *in vitro* diagnostic medical devices.
	Indicates the presence of the Radio Frequency Identification (RFID) reader/tag
	Total number of IVD tests that can be performed with the IVD medical device
	Indicates a carrier that contains unique device identifier information
	Importer
	Distributor
	UK conformity assessed under the Medical Devices Regulations 2002 (SI 2002 No 618, as amended) (UK MDR 2002)
	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. Kearon C. Diagnosis of suspected venous thromboembolism. Hematology. 2016.
3. Bruinstroop E, van de Ree MA, Huisman MV. The use of D-dimer in specific clinical conditions: a narrative review. Eur J Intern Med. 2009.
4. CLSI EP06-A
5. CLSI EP17-A2
6. CLSI EP5-A3
7. CLSI EP07-ED3

Visit www.CLSI.org for information

8. EMBOL-1 protocol – NCT04737954 https://www.clinicaltrials.gov/ct2/show/NCT04737954?term=LumiraDx&draw=2&rank=3
9. NICE Guideline (NG158): Venous thromboembolic diseases: diagnosis, management and thrombophilia testing https://www.nice.org.uk/guidance/ng158
10. Righini, M. et al. 2014. JAMA (2014) 311: 1117-1124. https://pubmed.ncbi.nlm.nih.gov/24643601/

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 on 00800 5864 7239 or by email: customerservices@lumiradx.com or at lumiradx.com.

If during the use of the device or as a result of its use, a serious incident has occurred, please report it to the manufacturer and/or its authorized representative and to your national authority.

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 agencies required 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 the Limited Warranty shall be made in writing within the applicable Limited Warranty period.

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Manufacturer information:

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