ENGLISH

lumiraDx™ INR Test

For Professional Use Only

SPEC-30809 R2 ART-00133 R4

LumiraDx INR Test

The LumiraDx INR 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.

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Intended use

The LumiraDx INR Test Strips are intended for use with the LumiraDx Instrument. It is for use by healthcare professionals for quantitative prothrombin time testing, reported as International Normalized Ratio (INR), for the monitoring of oral anticoagulation therapy with Vitamin-K Antagonist (VKA) drugs. The test uses fresh capillary blood. It is intended for use in patients 18 years of age or older.

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 INR Quality Control Pack Insert, and this entire product insert. In addition, please watch the LumiraDx Platform Training Video available at **www.lumiradx.com**.

Summary and explanation of the Test

International Normalized Ratio (INR) is a standardized measurement of the rate at which blood clots. It is calculated from the quantitative measurement of prothrombin time (PT) in capillary blood. A low INR can indicate an increased risk of blood clots, while an elevated INR can indicate increased risk of excessive bleeding[1].

Principle of the assay

The LumiraDx INR Test is a thrombin activation assay in which a quenched substrate is cleaved by thrombin and the emitting fluorescence is detected and quantified. When a blood sample is applied to the Test Strip, the clotting cascade that proceeds naturally leads to the conversion of prothrombin to thrombin which, subsequently, recognizes a peptide sequence on the substrate. Following cleavage of this peptide sequence, the substrate becomes unquenched and emits a fluorescent signal detectable by the LumiraDx Instrument. The amount of signal detected over a specific time is converted by means of an algorithm into standardized coagulation units (INR) and the result is displayed on the touch-screen.

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 Pack Insert

Materials required but not provided with the Test Strip carton

- LumiraDx Instrument
- LumiraDx INR Quality Controls (as required to meet local and organizational compliance)
- Standard blood collection equipment (lancets, biowaste disposal)
- LumiraDx Connect if connectivity required (refer to LumiraDx Connect User Manual)

Reagents: warnings and precautions

The Test Strip contains reagents designed to activate a cascade of coagulation in the applied sample and to generate an optical signal that can be used to measure the progress of that cascade. The key components of this reagent are a recombinant human tissue factor, synthetic phospholipids and a rhodamine-based substrate that can generate fluorescence. Reagents are 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 5°C and 32°C (41°F and 89°F). Avoid freezing or storing in any area that could exceed 32°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. You must use the Test Strip within 15 minutes of removing it from the foil pouch. 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 INR Test Strip:

- Capillary blood
- LumiraDx INR Quality Controls

Sample collection and preparation for analysis

When collecting any type of sample, follow universal blood collection precautions and guidelines according to your organization. The steps that follow apply to collecting a capillary blood sample from a finger stick. Optionally, you may use a non-anticoagulated Transfer Tube to collect the finger-stick blood sample. Details of recommended Transfer Tubes are available at **www.lumiradx.com.** Only auto-disabling, single use lancing devices may be used to collect capillary blood.

Procedure/performing a Test

Refer to the LumiraDx Platform User Manual for instructions on how to analyze a patient or Quality Control sample. The LumiraDx Platform Quick Reference Guide also provides an illustrated step by step procedure. Before running a LumiraDx INR Test Strip 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.

1. **Collecting a capillary blood sample from a finger stick:** Where possible, ensure the patient thoroughly washes and dries their hands prior to sample collection. **Note:** the hands should 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[2]. 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 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 touch-screen within 3 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

You may use a non-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.

Sample application using a transfer tube

Sample covering Sample Application Area

Built-in Controls

The LumiraDx Instrument and LumiraDx INR Test Strips have several quality control functions integrated to ensure validity of each test run. These checks ensure that the behavior 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 INR Test can be used with capillary 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 touch-screen of the LumiraDx Instrument. No INR value is reported in samples with Hct 'Out of Range'.

Quality Controls

Liquid Quality Controls are available from LumiraDx (**www.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 INR Test Strips, you must use the LumiraDx INR Quality Control. The Quality Controls come in two Levels. The frequency of testing will be determined by local guidelines. Refer to the LumiraDx INR 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.

Expected Results

The LumiraDx Instrument will display the results equivalent to laboratory plasma measurements as the International Normalized Ratio. Each Test Strip Lot is calibrated to a reference that is traceable to rTF/16 – the international reference for recombinant human thromboplastin. INR levels vary from person to person. Experience comparing results obtained with the LumiraDx INR Test to those obtained with common laboratory reagents shows that the LumiraDx INR Test correlates well with ACL Elite with Hemosil, RecombiPlasTin 2G. The LumiraDx INR Test may not correlate with other commercially available clinical laboratory reagents or instruments. Reference ranges for INR vary by laboratory, by instrument, or when using different reagents, therefore each physician should establish reference ranges and expected values for their own patient populations and individual patients. Other pre-analytical variables can also affect INR test results.

Limitations of the procedure

- The LumiraDx INR Test should not be used for patients being treated with any direct thrombin inhibitors, including Hirudin, Lepirudin, Bivalirudin, and Argatroban.
- The LumiraDx INR Test uses only fresh capillary whole blood. Venous blood, plasma or serum cannot be used. The blood drop must be a minimum of 8 µL 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.
- Hematocrit values between 25-55 % 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 INR result will be reported.
- The presence of anti-phospholipid antibodies (APAs) such as Lupus antibodies (LA) can potentially lead to prolonged clotting times, i.e., elevated INR values. A comparison to an APA-insensitive laboratory method is recommended if the presence of APAs is known or suspected.
- Interference may be observed from Fondaparinux in supratherapeutic patient samples with INR > 4.5. Fondaparinux concentrations up to 4mg/L showed no significant effect on results at therapeutic levels (INR 2-4.5).
- Refer to the LumiraDx Platform User Manual if an error message is displayed on the LumiraDx Instrument touch-screen.
- The LumiraDx INR Test results should be interpreted by a healthcare professional in conjunction with the patient's clinical presentation, history and other laboratory results. If the results are inconsistent with clinical evidence, additional testing is suggested to confirm the result.
- Certain over the counter or prescription medication or drugs may affect the result. Examples include analgesics, antibiotics, antidepressants, amiodarone, aspirin, azole antifungals, corticosteroids, direct-acting anti-virals, fibrates, glucosamine, non-steroidal anti-inflammatory drugs, statins, tamoxifen and thyroxine. Drugs known to reduce the INR include carbamazepine, griseofulvin, phenobarbital, phenytoin, primidone, rifampicin and St John's Wort[3]. When interpreting the result, the potential effect of underlying diseases (for example such as congestive heart failure, thyroid dysfunction or liver disease) should be considered. In addition, the potential effect of a drug interaction with the VKA must be considered.
- Changes in the patient's diet (e.g. alcohol consumption, the quantity of vitamin-K rich foods such as broccoli, kale or spinach, the use of cranberry or grapefruit juice, vitamin-K supplements [3]) can lead to unusually low or high results.
- 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, 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

Measuring range

The LumiraDx INR Test used with the LumiraDx Instrument has a reportable range of 0.8 – 7.5 INR.

Sensitivity

The LumiraDx INR Test is sensitive to various clotting factors as determined by *in vitro* tests. Four clotting factors were evaluated; Factor II, V, VII and X. Single factor depleted plasma was combined with a normal plasma pool to produce four series of diluted plasma samples. These plasma samples were then tested using one representative lot of LumiraDx INR Test Strips across 20 LumiraDx Instruments. The results, as seen in the table, represent the typical LumiraDx INR Test sensitivity to Factors II, V, VII, and X.

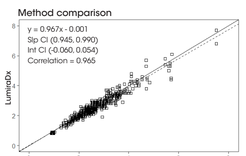
Clotting Factor	% Sensitivity
II	32.4
V	38.2
VII	55.0
X	55.3

Accuracy

596 capillary blood samples and venous blood samples were collected from 326 outpatients using 3 Test Strip lots across multiple sites. Finger stick capillary blood samples were measured on the LumiraDx Instrument with the LumiraDx INR Test using direct and Transfer Tube application. Venous plasma samples were measured on an ACL Elite Pro Coagulation Analyser with Hemosil RecombiPlasTin 2G. Results are as follows:

Fingerstick Capillary Direct Application Results from 3 Test Strip Lots at Multiple Sites

596 Capillary Blood Samples from 326 Patients



Sample application of capillary blood using a plastic non-anticoagulated Transfer Tube showed equivalent results to direct application from a fingerstick.

	n	Slope	Intercept	r
Direct Application	596	0.967	-0.001	0.965
Transfer Tube	598	0.955	0.015	0.958

Precision

Capillary blood precision was determined using duplicate samples from patients tested on 3 Test Strip lots at multiple sites. The following results represent the mean paired rep %CV for both direct and Transfer Tube application.

	n	Mean INR	Mean % CV
Direct Application	284	2.54	3.46
Transfer Tube	291	2.53	3.73

Interference

Testing was performed using whole blood samples spiked with interfering substances. The following interferents showed no significant effect on INR Test results (<10% difference compared to negative control with 95% confidence):

Interferent	Test Concentration
Acetylsalicylic Acid	0.652 g/L
Amlodipine	0.245 µmol/L
Bilirubin	0.2 g/L
Bisoprolol	0.92 µmol/L
Clopidogrel	7.5 x 10^{-2} g/L
Daptomycin	0.3 g/L
Furosemide	181 µmol/L
Hemoglobin	5 g/L
Lisinopril	0.74 µmol/L
Low Molecular Weight Heparin	2.0 IU/mL
Omeprazole	17.4 µmol/L
Paracetamol	1324 µmol/L
Salbutamol	1.67 µmol/L
Simvastatin	1.62 x 10^{-3} g/L
Lipemia (Triglycerides)	10.0 g/L
Unfractionated Heparin	1.5 IU/mL

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 fulfills 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. Keeling, D et al (2011) British Journal Haematology 154: 311-324.
2. Arline, K et al (2020) Point of Care 19: 12-18.
3. Clinical Knowledge Summary: anticoagulation-oral. National Institute for Clinical Excellence. Dec 2016

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 **www.lumiradx.com**.

For return policy

If there is a problem with the **LumiraDx INR 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 INR Test Strips – As per shelf life.

Unused 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 INR 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.

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 **www.lumiradx.com/IP**.

Legal notices

Manufacturer information

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