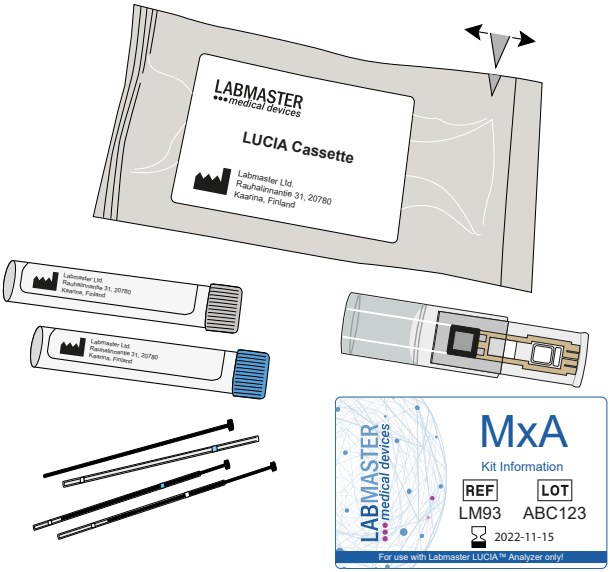
LABMASTER LUCIA

Instructions for Use

Labmaster LUCIA™ MxA Kit for Whole Blood Samples



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Labmaster LUCIA™ MxA Kit for Whole Blood Samples

Product number: LM93

1. Intended Use

Labmaster LUCIA™ MxA test is an *in vitro* near-patient diagnostic test for the quantitative determination of Myxovirus resistance protein A (MxA) from whole blood. The MxA test is used for detection of acute respiratory tract viral infections from symptomatic patients. The Labmaster LUCIA™ MxA Kit is to be used with semi-automated Labmaster LUCIA™ Analyzer by healthcare professionals.

2. Clinical Significance and Summary of the Test

MxA is an informative general biomarker for the most common acute viral infections as its levels in blood are increased with symptomatic respiratory viral infections. It can be used as a marker for distinguishing viral from bacterial disease. (i–v) This aids physicians in making the correct diagnosis and reduces unnecessary antibiotic treatment.

Measuring Range	Unit	Sample Volume	Sample Type	Measuring Time
50–1000	ng/mL	7 µL	Whole blood	11 minutes

3. Principle and Procedure

The Labmaster LUCIA™ MxA test is based on the formation of immunochemical complex between antibodies and the MxA analyte. There are two different MxA recognizing antibodies in the complex of which the capture antibody binds the analyte on the silicon chip of the LUCIA Cassette. Luminophore-labeled-antibody is dried in the MxA Reaction Tube where the sample is added with the MxA Lysis Solution. The labeled antibody reacts with MxA released from the lysed blood cells. The sample is added to the LUCIA Cassette where the unbound excess of the labeled antibody is separated with automatic washing step. Labeled antibody-analyte complex is excited with electricity. Resulting electrochemiluminescence is measured and the on-board microprocessor calculates the concentration of the analyte in the sample based on a pre-programmed calibration. The calculated and converted result is displayed on the screen of the Labmaster LUCIA™ Analyzer.

4. Kit Components

Contents of the Labmaster LUCIA™ MxA Kit for Whole Blood Samples

Component Name	Product Number LM93 (40 MxA tests)
MxA Cassette*	40 pcs
MxA Reaction Tube**	40 pcs (containing dried reagents)
MxA Lysis Solution***	600 µL x 2 pcs
MxA NFC Card	1 pc
Li-heparin coated capillaries (7 µL)	2 x 50 pcs
Capillaries (20 µL)	50 pcs
Plungers for capillaries	3 x 50 pcs
MxA Instructions for Use and Quick Guide (see centrefold)	1 pc

**Contains Tween, disodium tetraborate decahydrate, sodium azide, bovine serum albumin*
***Contains Tween, sodium azide, bovine serum albumin, bovine gamma globulin*
****Contains Tergitol™ 15-S-9*

Materials Required but Not Provided with the Kit

Product Name	Product Number
Labmaster LUCIA™ Analyzer	LM26
Labmaster LUCIA™ Analyzer Instructions for Use	LM28
Lancets for fingertip blood sample	N/A

Storage

Store LUCIA MxA Kit at +2 – +8°C. The MxA Cassettes together with MxA Reaction Tubes can be stored at room temperature for a maximum of three weeks after which they must be discarded. MxA Lysis Solution tubes can be stored in room temperature for a maximum of seven weeks. After initial opening of the MxA Lysis Solution tube, the MxA Lysis Solution can be used until the expiration date when stored as instructed.

Description of the Labmaster LUCIA™ MxA Cassette

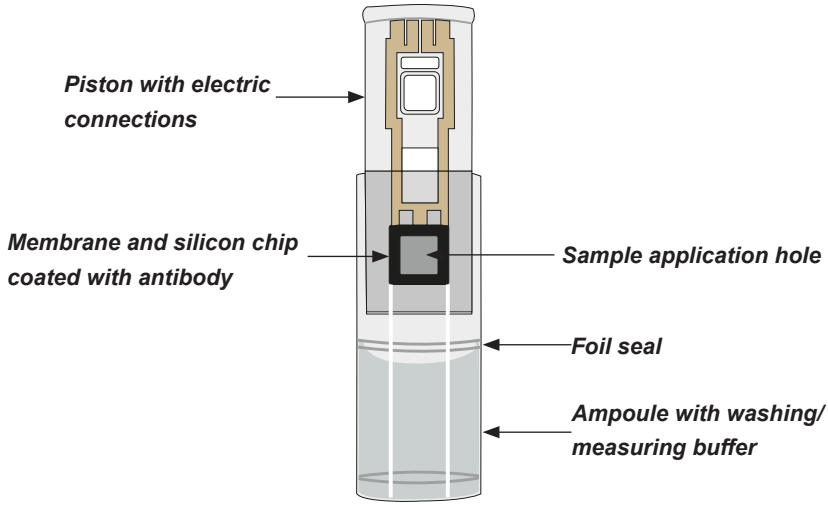

Figure 1.The Labmaster LUCIA™ MxA Cassette

5. Warnings and Precautions

Health and Safety Information

- For *in vitro* diagnostic use only.
- **Danger**: Washing/measuring buffer in cassette ampoule contains 1.7 mL of 1.9% disodium tetraborate decahydrate, which may damage fertility or the unborn child.

- MxA Lysis Solution contains 2% Tergitol™ 15-S-9 which is harmful if swallowed or inhaled, it causes skin irritation and serious eye damage (H302, H332, H315, H318).

- MxA Reaction Tubes and MxA Cassettes contain < 0.1% sodium azide, which is not considered a harmful amount.
- The kit should only be used by adequately trained personnel e.g., healthcare professional with formal education in a relevant healthcare or medical field.
- Wear protective clothing and single use laboratory gloves when handling the samples or performing the test. Wash hands properly after performing the test.

- Avoid contact of liquids with eyes and skin. If exposed, rinse immediately with plenty of water.
- All patient samples and controls should be handled as potentially infectious material.
- Cassette packaging contains a desiccant. This material shall not be used in the assay. Discard the desiccant.
- Disposal: See section 12.

Analytical Precautions

- The Labmaster LUCIA™ MxA Kit must be used only with the Labmaster LUCIA™ Analyzer.
- Do not use kit components after the expiry date printed on the kit label.
- Do not mix components with other kit batches.
- NFC Card is batch specific and should be used only for MxA tests from the same kit batch. If the NFC Card is lost, a new card can be requested from support@labmaster.fi.
- One MxA Lysis Solution tube is used for 20 LUCIA MxA tests. Avoid contamination and spillage of the MxA Lysis Solution tube content.
- Cassettes, reaction tubes, capillaries and plungers are for single use. Do not use already used cassettes, reaction tubes, capillaries or plungers.
- The MxA Cassette should not be used if the cassette pouch is damaged or broken, if the foil seal in a cassette ampoule has broken and washing/measuring buffer has leaked from ampoule, or if there is crystal formation on the cassette. Please see section 15.
- Note that the MxA Reaction Tube caps are intentionally left loose during the manufacturing process.
- Check that there are no air bubbles or foam in the cassette ampoule before use. If there are air bubbles, try to remove the bubbles by turning the cassette upside down or tapping the ampoule gently. If the liquid in the ampoule has foamed, do not use the cassette.
- Use cassette immediately after cassette pouch has been opened.
- After the measurement, if there is a large air bubble which covers the whole surface of the silicon chip of the cassette or if the chip is covered by the foil seal, the measurement result is unreliable.
- Do not use components of LUCIA MxA Kit if they have not been stored as instructed in this kit insert.
- Avoid contaminating the LUCIA Analyzer.
- There is a possibility that other substances and/or factors may interfere with the test and cause erroneous results (e.g. technical or procedural errors).

6. Sample Material and Collection

Note: MxA content in fingertip sample might differ from venous blood sample (v).

Sample Material	Sample Volume	Sample Collection
Fingertip sample (whole blood)	7 µL	Prick a clean and dry fingertip with a lancet and wipe away the first drop of blood. Aspirate the sample using a capillary, see section 7, Sample Pre-handling. The collected fingertip whole blood sample must be used immediately.
Anticoagulated whole blood	7 µL	Use venous blood sample collected in a tube containing EDTA or Li-heparin. Mix whole blood by inverting the tube several times. Collect the sample using a capillary or pipette, see section 7, Sample Pre-Handling. The collected venous whole blood must be measured within 2 days (48 h) when stored at +2 – +8°C.

7. Procedure

NOTE: Each LUCIA MxA Kit contains one batch specific NFC Card which is used for all tests in one kit. **Before measurement, ensure that the NFC Card batch information corresponds to MxA Cassette, MxA Reaction Tube and MxA Lysis Solution batch codes.**

Sample Pre-Handling

Both capillary (provided with the LUCIA MxA Kit) and pipette (not provided) can be used for sample transfer.

- Open the pouch containing MxA Cassette and MxA Reaction Tube and check that there are no small air bubbles or foam in the cassette ampoule. If there are small air bubbles, try to remove the bubbles by turning the cassette upside down or tapping the ampoule gently. If the liquid in the ampoule has foamed, do not use the cassette. After cassette ampoule has been checked and there are no small air bubbles or foam, use the cassette immediately.
- Place the plungers inside 20 µL (white marking) and 7 µL (blue marking) capillary tubes from the ends marked with colour.

- Mix the MxA Lysis Solution by gently inverting the tube a few times. Note that the MxA Lysis Solution foams easily.
- Fill the 20 µL capillary with MxA Lysis Solution up to the white stopper (see quick guide, step 1) or use pipette. The capillary will be filled faster if tilted or put all the way to the bottom of the tube. Make sure that the capillary is completely filled with liquid up to the white stopper. Small air bubbles in the capillary have no effect on the result.

- Dispense the MxA Lysis Solution to the bottom of the MxA Reaction Tube by pressing the plunger all the way down (see quick guide, step 2). Make sure that the capillary is completely empty. Sample has to be added to the MxA Reaction Tube within 15 minutes of the addition of MxA Lysis Solution.
- Fill the 7 µL capillary with the blood sample up to the white stopper or use pipette (see quick guide, step 3). Ensure that there are no air bubbles in the capillary.
- Dispense the blood sample to the bottom of the MxA Reaction Tube containing Lysis Solution, by pressing the plunger all the way down (see quick guide, step 4).
- **Mix the solution immediately with the capillary tip from the bottom of the tube** until the solution turns bright red (see quick guide, step 5). Mixing of the solution from the bottom of the tube is important for the dried reagents to dissolve. Make sure that the capillary is completely empty. If you are using pipette, mix by pipetting up and down from the bottom of the tube. Do not shake or invert the tube.
- Pre-handled sample is now ready to be measured.
- The pre-handled sample must be measured within 15 minutes of preparation.

Measurement

- Place a new plunger inside a new 7 µL capillary tube (blue marking).
- Select the patient sample measurement icon on LUCIA Analyzer's display, enter sample patient ID and read the NFC Card as instructed in Labmaster LUCIA™ Analyzer's Instructions for Use (see quick guide, step 6).
- Slide the cassette onto the tray of the analyzer from the right side of the tray (see quick guide, step 7). Note that the pre-handled sample has to be dispensed into the cassette during the 1-minute sample application time window after NFC Card has been read.
- Fill the 7 µL capillary with pre-handled sample up to the white stopper or use a pipette for sample transfer (see quick guide, step 8). The capillary will be filled faster if tilted.
- Place the capillary into the sample application hole of the cassette and hold the capillary against the membrane. Dispense the sample by pressing the plunger all the way down. Hold the capillary against the membrane until the sample has spread on the entire membrane (see quick guide, step 9).
- Start the measurement by selecting the Accept icon on the display (see quick guide, step 10). The measurement time is 11 minutes.
- When the measurement has been completed, the result will be shown on the analyzer's display (see quick guide, step 11) and the cassette will come out of the analyzer.
- Check that the silicon chip is not covered by large air bubble or by foil.
- Dispose the cassette immediately after use.
- Place the NFC Card and MxA Lysis Solution tube back into the kit box.

See the Labmaster LUCIA™ Analyzer's Instructions for Use for more detailed measurement instructions.

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LABMASTER LUCIA

A Point-of-care platform based on patented CECL technology

LABMASTER Ltd.
Rauhalinnantie 31,
20780 Kaarina, Finland | Tel. +358 22 760 555
www.labmaster.fi | E-mail: support@labmaster.fi

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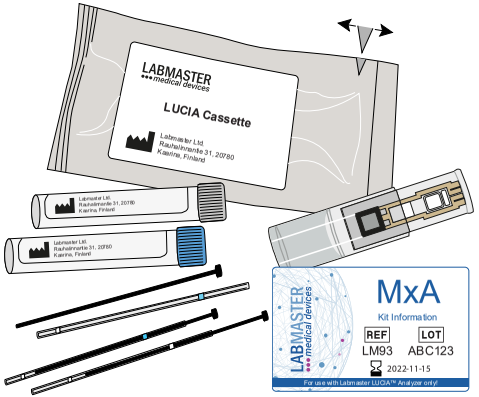
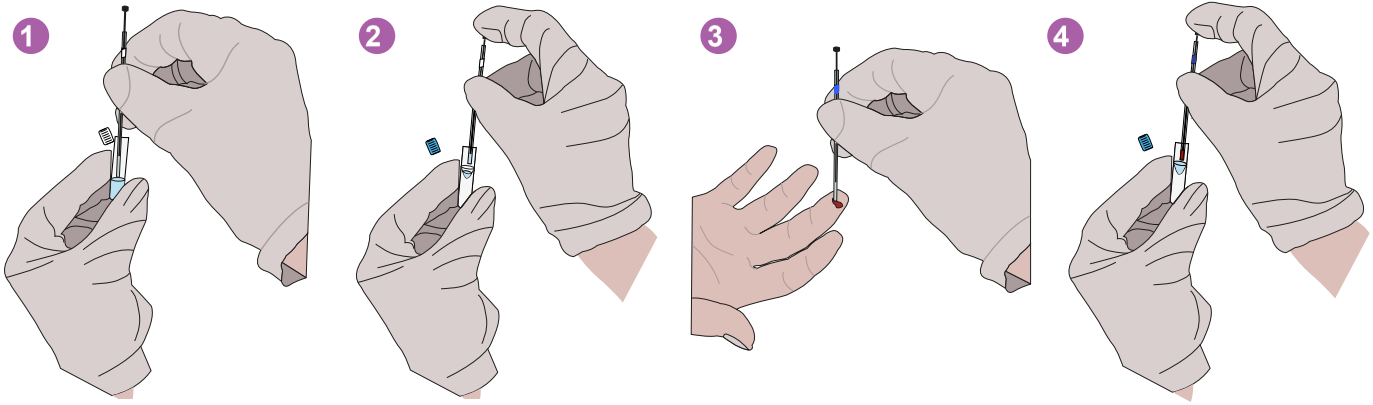
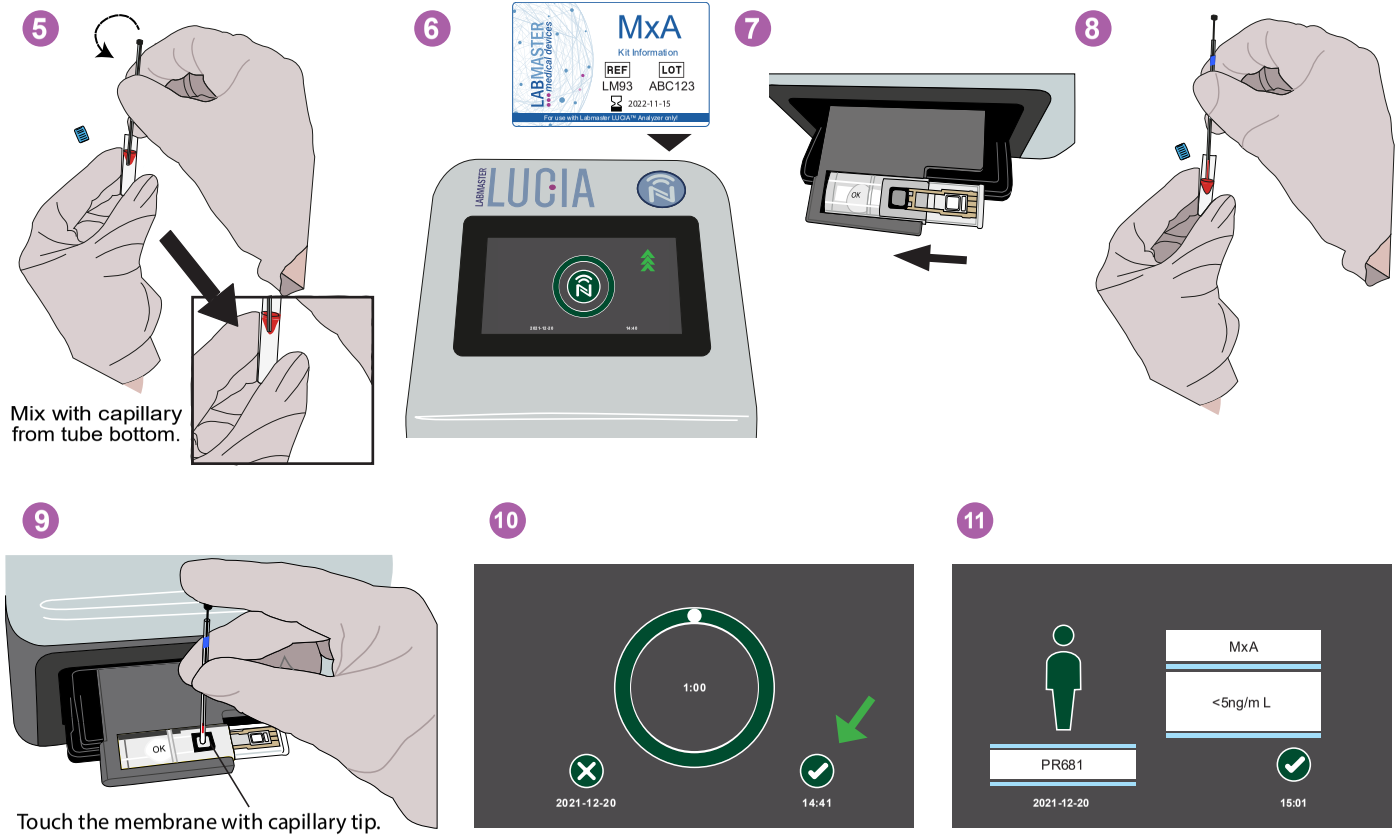
Labmaster LUCIA™ Analyzer



Components needed for one test:

- *1 cassette*
- *1 reaction tube*
- *1 lysis solution tube (used for 20 tests)*
- *1 capillary (20 µL) marked with white*
- *2 capillaries (7 µL) marked with blue*
- *3 plungers for capillaries*
- *1 NFC Card (used for all tests in the kit)*





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8. Quality Control

Both the Labmaster LUCIA™ Analyzer and LUCIA MxA test are factory calibrated. The use of control material is advised to assure the day-to-day validity of results. It is recommended that the customer prepares and measures own quality control materials regularly.

See the Labmaster LUCIA™ Analyzer's Instructions for Use for more detailed measurement instructions.

9. Interpretation of Results

When interpreting the LUCIA MxA test results, take into consideration the patient's medical history, clinical examinations and other laboratory results.

10. Limitations of the Procedure

Follow the sample collection, pre-handling and assay procedures specified in these instructions, otherwise the results might not be reliable. Test results should never be used alone for making a diagnosis. A clinical decision is always required.

Heterophilic antibodies in human serum/plasma are a well-recognized source of interference in immunoassays. They can react with immunoglobulins included in the assay components. Samples from patients routinely exposed to animals or animal serum products can demonstrate this type of interference potentially causing anomalous results (vi).

LUCIA MxA test is not intended for use for patients with cancer.

11. Performance Characteristics

Method Comparison

Method comparison of LUCIA MxA test was performed by measuring the same whole blood samples or samples collected at the same time from same patient with LUCIA MxA test and a reference method (in-house enzyme-linked immunosorbent assay at University of Turku). Clinical studies were performed at Turku University Hospital and the University of Turku. The regression line of method comparison was y = 0.5062x + 76.998 and correlation coefficient R = 0.77. The number of samples used for comparison study was 60.

Clinical Performance

Clinical performance was evaluated with 122 samples, consisting of 54 adults' samples and 68 children's (age 1 month – 17 years) samples. Since the MxA response during infections in adults and children is different, following cut-off values were used in clinical performance calculations; 50 ng/mL for adults and 110 ng/mL for children measured with LUCIA MxA test, and 70 ng/mL for adults and 160 ng/mL for children measured with the reference method.

Clinical specificity	98%
Clinical sensitivity	91%
Clinical accuracy	93%
Positive predictive value PPV	99%
Negative predictive value NPV	85%

Measuring Range

LUCIA MxA test is used for measuring MxA with a range of 50–1000 ng/mL from whole blood sample. The sample is diluted and lysed before measurement. MxA < 50 ng/mL is displayed if the MxA concentration is below the measuring range. MxA > 1000 ng/mL is displayed if the MxA concentration is above the measuring range. The measurement procedure shows linearity for the interval from 50 to 1000 ng/mL, with deviations from linearity within ±10% (evaluated according to CLSI document EP06-Ed2, vii).

Precision

The precision of LUCIA MxA test was determined with single-site 20 x 2 x 2 precision evaluation protocol according to guidelines in CLSI document EP05-A3 (viii), by measuring three samples twice per run, two runs per day, for 20 testing days by three operators, using a single analyzer and reagent batch. Two of the samples were in-house QC material of lyophilized whole blood and one sample was in-house standard of native MxA in lyophilized whole blood.

Sample	Mean Value	N	Repeatability		Between-Run		Between-Day		Within-Laboratory	
			SD	CV%	SD	CV%	SD	CV%	SD	CV%
Level 1	139	80	18	13%	N/A	N/A	15	11%	23	17%
Level 2	917	80	85	9%	8	1%	73	8%	112	12%
Standard	146	80	16	11%	17	11%	15	10%	27	19%

Reproducibility

Reproducibility for the MxA test kit on the LUCIA Analyzer was determined from Li-heparin whole blood by applying CLSI guideline EP05-A3 (viii). One whole blood sample was measured as five replicates, during one day, by two operators, using five LUCIA analyzers and three cassette lots (total n=75).

Sample Matrix	Mean Value	N	Repeatability		Between-Lot		Between-Analyzer		Reproducibility	
			SD	CV%	SD	CV%	SD	CV%	SD	CV%
Lithium-heparin whole blood	171	75	28	16%	7	4%	16	9%	33	19%

Detection Capability

The limit of detection (LoD) for MxA is 18 ng/mL, determined consistent with the guidelines in CLSI document EP17-A2 based on the proportions of false positives (α) less than 5% and false negatives (β) less than 5%; using 240 determinations, with 120 blank and 120 low level samples; and a limit of blank (LoB) of 6 ng/mL (ix).

The limit of quantitation (LoQ) for MxA is 41 ng/mL, estimated according to the guidelines in CLSI document EP17-A2, based on 118 LoD determinations; and a target accuracy goal of 19% total error (ix).

Interfering Substances

The following substances, when tested in whole blood at low and high MxA concentrations, were found not to interfere at the concentrations indicated. A bias exceeding 20% is considered a significant interference. Over 1.5 g/L cholesterol increases the MxA response measured with LUCIA MxA test when MxA is present in the sample. The MxA test was evaluated for interference according to guidelines in CLSI guideline EP07-A2 (x).

Substance	No Interference Found up to Concentration
Unconjugated bilirubin	20 mg/dL
Conjugated bilirubin	33 mg/dL
Triglycerides	3300 mg/dL
Cholesterol	1.5 g/L
Ascorbic acid (vitamin C)	60 mg/L
EDTA	1.25 mg/L
Heparin	10 000 U/L

12. Disposal

All patient samples and materials shall be disposed of according to local laws and regulations. All samples, used cassettes, capillary tubes, plungers, pipette tips and reaction tubes shall be disposed of as biological, potentially infectious materials. Paper, carton and pouches from LUCIA MxA Kit can be recycled according to local and national instructions. Desiccants and NFC Card can be disposed of in general waste. This product will not cause any health risk if used in accordance with the Instructions for Use.

13. Notice on Reporting Serious Incidents

For a patient/user/third party in the European Union and in countries with identical regulatory regime (Regulation 2017/746/EU on In vitro Diagnostic Medical Devices); if, during the use of this 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.

14. Warranty

The performance data presented here were obtained using the assay procedure indicated. Any change or modification of the procedure not recommended by Labmaster Ltd. may affect the results.

In which event it disclaims all warranties expressed, implied or statutory including the implied warranty of merchantability and fitness for use and shall not be liable for damages indirect or consequential.

15. Troubleshooting

For Analyzer-related questions see Labmaster LUCIA™ Analyzer (LM26) Instructions for Use (LM28).

Indication	Probable Causes	Corrective Action
• Washing/measuring buffer has leaked from ampoule or there is crystal formation on the cassette.	• Foil seal in the cassette ampoule has broken.	• Do not use the cassette. • If the problem reoccurs, contact support@labmaster.fi
• Washing/measuring buffer inside the cassette has foamed.	• Cassette has been handled heavy-handedly or cassette has been dropped.	• Do not use the cassette. • If the problem reoccurs, contact support@labmaster.fi

• Sample does not go through membrane.	• Kit has not been stored at the instructed storage temperature or the cassette pouch has broken. • Cassette has been taken out of the pouch too early.	• Do not use the cassette. • If the problem reoccurs, contact support@labmaster.fi
• Liquid residue on the tray.	• Washing/measuring buffer has leaked from ampoule.	• Blot the liquid into a soft paper or cloth. • If the problem reoccurs, contact support@labmaster.fi
• Rejected measurement.	• Air bubble or foil seal on top of silicon chip. • Air bubbles or foam in washing/measuring buffer.	• Repeat the measurement using a new MxA Cassette. • If the problem reoccurs, contact support@labmaster.fi
• Grinding sound during tray movement.	• Mechanical malfunction. • Cassette is placed on the tray incorrectly.	• Restart the LUCIA Analyzer. • Repeat the measurement using a new MxA Cassette. • If the problem reoccurs, contact support@labmaster.fi
• Foil seal covers the silicon chip after measurement.	• Defective cassette.	• Measurement result is unreliable, do not use the result. • Repeat the measurement using a new MxA Cassette. • If the problem reoccurs, contact support@labmaster.fi

16. References

i. Engelmann I., Dubos F., Lobert P.E., Houssin C., Degas V., Sardet A., Decoster A., Dewilde A., Martinot A, and Hober D. 2015. Diagnosis of viral infections using myxovirus resistance protein A (MxA). Pediatrics 135:e985–993.

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iii. Ivaska L. 2017. Diagnostic studies in children with acute infections: Microbes and biomarkers. Doctoral thesis. Annales Universitatis Turkuensis series D, part 1269, University of Turku, Finland.

iv. Toivonen L. 2016. Rhinovirus infections in young children: Clinical manifestations, susceptibility, and host response. Doctoral thesis. Annales Universitatis Turkuensis series D, part 1249, University of Turku, Finland.

v. Chieux V., Hober D., Chehadeh W., Harvey J., Alm G., Cousin J., Ducoulombier H. and Wattre, P. 1999. MxA protein in capillary blood of children with viral infections. J Med Virol 59:547–551.

vi. Clinical and Laboratory Standards Institute (CLSI) guideline I/LA30-A.

vii. Clinical and Laboratory Standards Institute (CLSI) guideline EP06-Ed2.

viii. Clinical and Laboratory Standards Institute (CLSI) guideline EP05-A3.

ix. Clinical and Laboratory Standards Institute (CLSI) guideline: EP17-A2.

x. Clinical and Laboratory Standards Institute (CLSI): guideline EP07-A2.

17. Explanation of Symbols

Symbol	Description
	The CE marking Conformity to the European directive 98/79/EC on in vitro diagnostic medical devices
	Manufacturer
	Use by date (YYYY-MM-DD)
	Temperature limit

	Do not reuse
	Consult Instructions for Use
	Catalog number
	Batch code
	In vitro Diagnostic medical device
	Contents sufficient for <n> tests
	Serious health hazard
	Harmful if swallowed or inhaled and causes skin irritation
	Causes serious eye damage
	Caution

Labmaster Ltd.
Rauhalinnantie 31 | 20780 Kaarina | Finland
Tel: +358 22 760 555 | Email: support@labmaster.fi

CE
IVD