

Lactate Dehydrogenase acc. to IFCC ver.2**Order information**

REF	CONTENT	Analyzer(s) on which cobas c pack(s) can be used
03004732 122	Lactate Dehydrogenase acc. to IFCC ver.2 (300 tests)	System-ID 07 6607 0 Roche/Hitachi cobas c 311, cobas c 501/502
Materials required (but not provided):		
10759350 190	Calibrator f.a.s. (12 x 3 mL)	Code 401
10759350 360	Calibrator f.a.s. (12 x 3 mL, for USA)	Code 401
12149435 122	Precinorm U plus (10 x 3 mL)	Code 300
12149435 160	Precinorm U plus (10 x 3 mL, for USA)	Code 300
12149443 122	Precipath U plus (10 x 3 mL)	Code 301
12149443 160	Precipath U plus (10 x 3 mL, for USA)	Code 301
05117003 190	PreciControl ClinChem Multi 1 (20 x 5 mL)	Code 391
05947626 190	PreciControl ClinChem Multi 1 (4 x 5 mL)	Code 391
05947626 160	PreciControl ClinChem Multi 1 (4 x 5 mL, for USA)	Code 391
05117216 190	PreciControl ClinChem Multi 2 (20 x 5 mL)	Code 392
05947774 190	PreciControl ClinChem Multi 2 (4 x 5 mL)	Code 392
05947774 160	PreciControl ClinChem Multi 2 (4 x 5 mL, for USA)	Code 392
04489357 190	Diluent NaCl 9 % (50 mL)	System-ID 07 6869 3

English**System information**

For **cobas c** 311/501 analyzers:

LDHI2: ACN 080

LDIP2: ACN 147 (with automatic sample pre-dilution)^{a)}

For **cobas c** 502 analyzer:

LDHI2: ACN 8080

LDIP2: ACN 8147 (with automatic sample pre-dilution)^{a)}

a) Not available in the US

Intended use

In vitro test for the quantitative determination of lactate dehydrogenase in human serum and plasma on Roche/Hitachi **cobas c** systems.

Summary^{1,2,3,4,5,6}

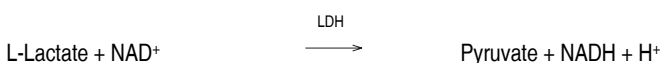
The lactate dehydrogenase (LDH) enzyme is widely distributed in tissue, particularly in the heart, liver, muscles and kidneys. The LDH in serum can be separated into five different isoenzymes based on their electrophoretic mobility. Each isoenzyme is a tetramer composed of two different subunits. These two subunits have been designated heart and muscle, based on their polypeptide chains. There are two homotetramers, LDH-1 (heart) and LDH-5 (muscle), and three hybrid isoenzymes.

Elevated serum levels of LDH have been observed in a variety of disease states. The highest levels are seen in patients with megaloblastic anemia, disseminated carcinoma and shock. Moderate increases occur in muscular disorders, nephrotic syndrome and cirrhosis. Mild increases in LDH activity have been reported in cases of myocardial or pulmonary infarction, leukemia, hemolytic anemia and non-viral hepatitis.

The method described here is derived from the formulation recommended by the IFCC^{5,6} and was optimized for performance and stability.

Test principle**UV assay**

Lactate dehydrogenase catalyzes the conversion of L-lactate to pyruvate; NAD is reduced to NADH in the process.



The initial rate of the NADH formation is directly proportional to the catalytic LDH activity. It is determined by photometrically measuring the increase in absorbance.

Reagents - working solutions

R1 N-methylglucamine: 400 mmol/L, pH 9.4 (37 °C); lithium lactate: 62 mmol/L; stabilizers

R2 NAD: 62 mmol/L; stabilizers; preservatives

R1 is in position B and R2 is in position C.

Precautions and warnings

For in vitro diagnostic use for health care professionals. Exercise the normal precautions required for handling all laboratory reagents.

Infectious or microbial waste:

Warning: handle waste as potentially biohazardous material. Dispose of waste according to accepted laboratory instructions and procedures.

Environmental hazards:

Apply all relevant local disposal regulations to determine the safe disposal.

Safety data sheet available for professional user on request.

For USA: Caution: Federal law restricts this device to sale by or on the order of a physician.

This kit contains components classified as follows in accordance with the Regulation (EC) No. 1272/2008:

**Warning**

H317 May cause an allergic skin reaction.

Prevention:

P261 Avoid breathing dust/fume/gas/mist/vapours/spray.

P272 Contaminated work clothing should not be allowed out of the workplace.

P280 Wear protective gloves.

Response:

P333 + P313 If skin irritation or rash occurs: Get medical advice/attention.

P362 + P364 Take off contaminated clothing and wash it before reuse.

Disposal:

P501 Dispose of contents/container to an approved waste disposal plant.

Product safety labeling follows EU GHS guidance.

Contact phone: all countries: +49-621-7590, USA: 1-800-428-2336

Reagent handling

Ready for use

Storage and stability*LDHI2, LDIP2*

Shelf life at 2-8 °C: See expiration date on **cobas c** pack label.

On-board in use and refrigerated on the analyzer: 12 weeks

Diluent NaCl 9 %

Shelf life at 2-8 °C: See expiration date on **cobas c** pack label.

On-board in use and refrigerated on the analyzer: 12 weeks

Specimen collection and preparation

For specimen collection and preparation only use suitable tubes or collection containers.

Only the specimens listed below were tested and found acceptable.
Serum.

Plasma: Li-heparin plasma.

Caution: Plasma from primary tubes handled according to the manufacturer's instructions can still contain cells, leading to implausibly high results. One option for these cases is an application with automatic sample pre-dilution (ACN 147/ACN 8147). Alternatively it is recommended to transfer the plasma from the primary tube to a secondary sample tube.

The sample types listed were tested with a selection of sample collection tubes that were commercially available at the time of testing, i.e. not all available tubes of all manufacturers were tested. Sample collection systems from various manufacturers may contain differing materials which could affect the test results in some cases. When processing samples in primary tubes (sample collection systems), follow the instructions of the tube manufacturer.

Separate the serum or plasma from the clot or cells promptly.

Centrifuge samples containing precipitates before performing the assay.

See the limitations and interferences section for details about possible sample interferences.

Sample stability claims were established by experimental data by the manufacturer or based on reference literature and only for the temperatures/time frames as stated in the method sheet. It is the responsibility of the individual laboratory to use all available references and/or its own studies to determine specific stability criteria for its laboratory.

Stability:⁷ 7 days at 15-25 °C

The sample may be stored for 4 days at 2-8 °C or 6 weeks at -20 °C. In connection with certain diseases (e.g. hepatopathy, diseases of skeletal muscle, malignant tumors), the LDH-4 and LDH-5 isoenzyme portions are increased and unstable in cooled and frozen samples; this may lead to an incorrect LDH value in samples collected from patients suffering from such diseases.

Materials provided

See "Reagents – working solutions" section for reagents.

Materials required (but not provided)

- See "Order information" section
- General laboratory equipment

Assay

For optimum performance of the assay follow the directions given in this document for the analyzer concerned. Refer to the appropriate operator's manual for analyzer-specific assay instructions.

The performance of applications not validated by Roche is not warranted and must be defined by the user.

Application for serum and plasma**cobas c 311 test definition**

Assay type	Rate A		
Reaction time / Assay points	10 / 20-33		
Wavelength (sub/main)	700/340 nm		
Reaction direction	Increase		
Units	U/L (µkat/L)		
Reagent pipetting		Diluent (H ₂ O)	
R1	100 µL	–	
R2	20 µL	–	
<i>Sample volumes LDHI2</i>	<i>Sample</i>	<i>Sample dilution</i>	
		Sample	Diluent (H ₂ O)
Normal	2.8 µL	–	–
Decreased	1.1 µL	–	–
Increased	2.8 µL	–	–
<i>Sample volumes LDIP2</i>	<i>Sample</i>	<i>Sample dilution</i>	
		Sample	Diluent (NaCl)
Normal	14 µL	20 µL	80 µL
Decreased	5.6 µL	20 µL	80 µL
Increased	14 µL	20 µL	80 µL

cobas c 501 test definition

Assay type	Rate A		
Reaction time / Assay points	10 / 28-47		
Wavelength (sub/main)	700/340 nm		
Reaction direction	Increase		
Units	U/L (µkat/L)		
Reagent pipetting		Diluent (H ₂ O)	
R1	100 µL	–	
R2	20 µL	–	
<i>Sample volumes LDHI2</i>	<i>Sample</i>	<i>Sample dilution</i>	
		Sample	Diluent (H ₂ O)
Normal	2.8 µL	–	–
Decreased	1.1 µL	–	–
Increased	2.8 µL	–	–
<i>Sample volumes LDIP2</i>	<i>Sample</i>	<i>Sample dilution</i>	
		Sample	Diluent (NaCl)
Normal	14 µL	20 µL	80 µL
Decreased	5.6 µL	20 µL	80 µL
Increased	14 µL	20 µL	80 µL

cobas c 502 test definition

Assay type	Rate A		
Reaction time / Assay points	10 / 28-47		
Wavelength (sub/main)	700/340 nm		
Reaction direction	Increase		
Units	U/L (µkat/L)		
Reagent pipetting		Diluent (H ₂ O)	
R1	100 µL	–	
R2	20 µL	–	

Sample volumes LDHI2	Sample	Sample dilution	
		Sample	Diluent (H ₂ O)
Normal	2.8 µL	–	–
Decreased	1.1 µL	–	–
Increased	5.6 µL	–	–
Sample volumes LDIP2	Sample	Sample dilution	
		Sample	Diluent (NaCl)
Normal	14 µL	20 µL	80 µL
Decreased	5.6 µL	20 µL	80 µL
Increased	20 µL	20 µL	80 µL

Calibration

Calibrators	S1: H ₂ O
	S2: C.f.a.s.
Calibration mode	Linear
Calibration frequency	2-point calibration
	• after reagent lot change
	• as required following quality control procedures

Calibration interval may be extended based on acceptable verification of calibration by the laboratory.

Traceability: This method has been standardized against the original IFCC[®] formulation using calibrated pipettes together with a manual photometer providing absolute values and the substrate-specific absorptivity, *c*.

Quality control

For quality control, use control materials as listed in the "Order information" section.

In addition, other suitable control material can be used.

The control intervals and limits should be adapted to each laboratory's individual requirements. Values obtained should fall within the defined limits. Each laboratory should establish corrective measures to be taken if values fall outside the defined limits.

Follow the applicable government regulations and local guidelines for quality control.

Calculation

Roche/Hitachi **cobas c** systems automatically calculate the analyte activity of each sample.

Conversion factor: U/L x 0.0167 = µkat/L

Limitations - interference

Criterion: Recovery within ± 10 % of initial value at a lactate dehydrogenase activity of 200 U/L (3.34 µkat/L).

Icterus:⁸ No significant interference up to an I index of 60 for conjugated and unconjugated bilirubin (approximate conjugated and unconjugated bilirubin concentration: 1026 µmol/L or 60 mg/dL).

Hemolysis:⁸ No significant interference up to an H index of 15 (approximate hemoglobin concentration: 9.6 µmol/L or 15 mg/dL).

Contamination with erythrocytes will elevate results, because the analyte level in erythrocytes is higher than in normal sera. The level of interference may be variable depending on the content of analyte in the lysed erythrocytes.

Lipemia (Intralipid):⁹ No significant interference up to an L index of 900. There is poor correlation between the L index (corresponds to turbidity) and triglycerides concentration.

Drugs: No interference was found at therapeutic concentrations using common drug panels.^{9,10}

In very rare cases, gammopathy, in particular type IgM (Waldenström's macroglobulinemia), may cause unreliable results.¹¹

For diagnostic purposes, the results should always be assessed in conjunction with the patient's medical history, clinical examination and other findings.

ACTION REQUIRED

Special Wash Programming: The use of special wash steps is mandatory when certain test combinations are run together on Roche/Hitachi **cobas c** systems. The latest version of the carry-over evasion list can be found with the NaOHD-SMS-SmpCin1+2-SCCS Method Sheets. For further instructions refer to the operator's manual. **cobas c** 502 analyzer: All special wash programming necessary for avoiding carry-over is available via the **cobas** link, manual input is required in certain cases.

Where required, special wash/carry-over evasion programming must be implemented prior to reporting results with this test.

Limits and ranges**Measuring range**

10-1000 U/L (0.17-16.7 µkat/L)

Determine samples having higher activities via the rerun function. Dilution of samples via the rerun function is a 1:2.5 dilution. Results from samples diluted using the rerun function are automatically multiplied by a factor of 2.5.

Lower limits of measurement

Lower detection limit of the test

10 U/L (0.17 µkat/L)

The lower detection limit represents the lowest measurable analyte level that can be distinguished from zero. It is calculated as the value lying 3 standard deviations above that of the lowest standard (standard 1 + 3 SD, repeatability, n = 21).

Expected values

Acc. to IFCC measured at 37 °C:¹²

Females	135-214 U/L	(2.25-3.55 µkat/L)
Males	135-225 U/L	(2.25-3.75 µkat/L)
Children (2-15 y)	120-300 U/L	(2.00-5.00 µkat/L)
Newborns (4-20 d)	225-600 U/L	(3.75-10.0 µkat/L)

Consensus values:¹³

Males & Females	up to 250 U/L	(up to 4.2 µkat/L)
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Each laboratory should investigate the transferability of the expected values to its own patient population and if necessary determine its own reference ranges.

Roche has not evaluated reference ranges in a pediatric population.

Specific performance data

Representative performance data on the analyzers are given below. Results obtained in individual laboratories may differ.

Precision

Precision was determined using human samples and controls in an internal protocol with repeatability (n = 21) and intermediate precision (3 aliquots per run, 1 run per day, 21 days). The following results were obtained:

LDHI2

Repeatability	Mean	SD	CV
	U/L (µkat/L)	U/L (µkat/L)	%
Precinorm U	164 (2.74)	1 (0.02)	0.8
Precipath U	263 (4.39)	2 (0.03)	0.7
Human serum 1	122 (2.04)	2 (0.03)	1.3
Human serum 2	396 (6.61)	4 (0.07)	0.9
Intermediate precision	Mean	SD	CV
	U/L (µkat/L)	U/L (µkat/L)	%
Precinorm U	159 (2.66)	2 (0.03)	1.0
Precipath U	260 (4.34)	2 (0.03)	0.9
Human serum 3	117 (1.95)	3 (0.05)	2.7
Human serum 4	323 (5.39)	4 (0.07)	1.1

LDIP2

Repeatability	Mean	SD	CV
	U/L (µkat/L)	U/L (µkat/L)	%
Precinorm U	166 (2.77)	1 (0.02)	0.6
Precipath U	268 (4.48)	1 (0.02)	0.4
Human serum 1	125 (2.09)	1 (0.02)	1.1
Human serum 2	402 (6.71)	3 (0.05)	0.7
Intermediate precision	Mean	SD	CV
	U/L (µkat/L)	U/L (µkat/L)	%
Precinorm U	168 (2.81)	2 (0.03)	1.1
Precipath U	272 (4.54)	3 (0.05)	0.9
Human serum 3	124 (2.07)	3 (0.05)	2.7
Human serum 4	340 (5.68)	4 (0.07)	1.2

The data obtained on **cobas c 501** analyzer(s) are representative for **cobas c 311** analyzer(s).

Method comparison

LDH values for human serum and plasma samples obtained on a Roche/Hitachi **cobas c 501** analyzer (y) were compared with those determined using the corresponding reagent on a Roche/Hitachi 917 analyzer (x).

LDH12

Sample size (n) = 86

Passing/Bablok¹⁴

$$y = 1.000x + 4.40 \text{ U/L}$$

$$r = 0.982$$

The sample activities were between 100 and 935 U/L (1.67 and 15.6 µkat/L).

LDIP2

Sample size (n) = 86

Passing/Bablok¹⁴

$$y = 1.000x + 6.82 \text{ U/L}$$

$$r = 0.975$$

The sample activities were between 89.8 and 950 U/L (1.50 and 15.9 µkat/L).

The data obtained on **cobas c 501** analyzer(s) are representative for **cobas c 311** analyzer(s).

References

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A point (period/stop) is always used in this Method Sheet as the decimal separator to mark the border between the integral and the fractional parts of a decimal numeral. Separators for thousands are not used.

Any serious incident that has occurred in relation to the device shall be reported to the manufacturer and the competent authority of the Member State in which the user and/or the patient is established.

Symbols

Roche Diagnostics uses the following symbols and signs in addition to those listed in the ISO 15223-1 standard:

CONTENT

Contents of kit



Volume after reconstitution or mixing

GTIN

Global Trade Item Number

FOR US CUSTOMERS ONLY: LIMITED WARRANTY

Roche Diagnostics warrants that this product will meet the specifications stated in the labeling when used in accordance with such labeling and will be free from defects in material and workmanship until the expiration date printed on the label. THIS LIMITED WARRANTY IS IN LIEU OF ANY OTHER WARRANTY, EXPRESS OR IMPLIED, INCLUDING ANY IMPLIED WARRANTY OF MERCHANTABILITY OR FITNESS FOR PARTICULAR PURPOSE. IN NO EVENT SHALL ROCHE DIAGNOSTICS BE LIABLE FOR INCIDENTAL, INDIRECT, SPECIAL OR CONSEQUENTIAL DAMAGES.

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