LACT2

cobas®

Lactate Gen.2

Order information

REF		CONTENT		Analyzer(s) on which **cobas c** pack(s) can be used
08057940190	08057940500	Lactate Gen.2 (100 tests)	System-ID 2079 001	**cobas c** 303, **cobas c** 503, **cobas c** 703

Materials required (but not provided):

10759350190	Calibrator f.a.s. (12 x 3 mL)	Code 20401	
05117003190	PreciControl ClinChem Multi 1 (20 x 5 mL)	Code 20391	
05947626190	PreciControl ClinChem Multi 1 (4 x 5 mL)	Code 20391	
05117216190	PreciControl ClinChem Multi 2 (20 x 5 mL)	Code 20392	
05947774190	PreciControl ClinChem Multi 2 (4 x 5 mL)	Code 20392	
08063494190	Diluent NaCl 9 % (123 mL)	System-ID 2906 001	

English

System information

LACT2C: ACN 20790 (CSF)

LACT2P: ACN 20791 (Plasma)

Intended use

In vitro test for the quantitative determination of lactate in human plasma and CSF on **cobas c** systems.

Summary

Lactate measurements, performed with this assay, in human plasma and cerebrospinal fluid (CSF), are used for the diagnosis and for monitoring of lactic acidosis.

Lactate is an intermediate in carbohydrate metabolism. It is mainly derived from white skeletal muscle, brain, skin, renal medulla and erythrocytes. Glucose is converted to lactate in the periphery by glycolysis, and re-conversion of lactate to glucose occurs mainly in the liver by gluconeogenesis. The balance between lactate production and lactate metabolism determines the blood concentration of lactic acid, with hyperlactatemia occurring when lactate production exceeds lactate consumption. Anaerobic glycolysis markedly increases blood lactate, especially with prolonged exercise.[1]

Lactic acidosis (accumulation of lactate and protons in the body) can occur in 2 main clinical settings:[2]

- Type A: cases of decreased tissue oxygenation and perfusion such as shock, sepsis, pneumonia, hypovolemia, congestive heart failure.[2]
- Type B: cases of hyperlactatemia without evidence of tissue hypoxia. Mostly associated with underlying diseases (e.g. diabetes mellitus, neoplasia, liver disease), with common drugs and/or toxins (e.g., ethanol, methanol, salicylates, antiretroviral agents, propofol), or with inborn errors of metabolism (e.g., methylmalonic aciduria, propionic acidemia, fatty acid oxidation defects). Thiamine deficiency can also be associated with lactic acidosis as thiamine is an important cofactor for aerobic glycolysis.[2]

CSF lactate concentration depends largely on its production from central nervous system (CNS) glycolysis. Raised levels of CSF lactate may occur within a range of CNS pathologies, including intracranial infection, seizures (in particular status epilepticus and focal seizures with loss of awareness), stroke and mitochondrial disorders, and any clinical condition associated with reduced oxygenation of the brain.[3] CSF lactate is elevated in both bacterial and fungal meningitis, but not in viral meningitis.[4]

Over the years, enzymatic methods for the determination of lactate have gained favor over colorimetric and titrimetric methods. Several different methods have been described for the determination of lactate.[5,6] The method presented here uses an enzymatic reaction to convert lactate to pyruvate. The hydrogen peroxide produced by this reaction is then used in an enzymatic reaction to generate a colored dye.[7,8]

Test principle

Colorimetric assay.

L-lactate is oxidized to pyruvate by the specific enzyme lactate oxidase (LOD). Peroxidase (POD) is used to generate a colored dye using the hydrogen peroxide generated in the first reaction.[7,8]

$$\text{L-lactate} + O_2 \xrightarrow{\text{LOD}} \text{pyruvate} + H_2O_2$$

$$2\ H_2O_2 + \text{H donor} + \text{4-AAP} \xrightarrow{\text{POD}} \text{chromogen} + 2\ H_2O$$

The intensity of the color formed is directly proportional to the L-lactate concentration. It is determined by measuring the increase in absorbance.

Reagents - working solutions

R1 Hydrogen donor: 1.75 mmol/L; ascorbate oxidase (cucumber): 501 µkat/L; buffers; preservatives

R3 4-Aminoantipyrine: 5 mmol/L; lactate oxidase (microbial): 251 µkat/L; peroxidase (horseradish): 401 µkat/L; buffers; preservatives

R1 is in position B and R3 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.

Reagent handling

Ready for use

Storage and stability

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: **Do not use serum specimens.**
Plasma: Na-fluoride/K-oxalate and Na-fluoride/Na-heparin plasma. Centrifuge within 15 minutes of collecting the specimen.
CSF: May be used as obtained.

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.

Centrifuge samples containing precipitates before performing the assay.

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

Note

1. The lactate level increases rapidly with physical exercise. The time required for return to normal lactate values depends on the physical fitness of the subject. 30 minutes at rest is usually sufficient for this purpose.
2. Blood samples should be drawn from a stasis-free vein. However, minimal hemostasis (less than 30 seconds) will not affect lactate levels. Avoid the use of a tourniquet, if possible.[9]
3. Glycolysis in blood samples can rapidly increase lactate levels. Cells contribute to the glycolysis and their quick removal is essential for accurate lactate analysis.[10] Heparinized plasma is acceptable, but precautions must be taken to retard glycolysis by keeping the whole blood on ice and then separating the plasma from the cells within 15 minutes of collection.

Stability in plasma (separated):[11]	8 hours at 15-25 °C
	14 days at 2-8 °C
Stability in plasma (heparinized):[12]	38 days at -20 °C (± 5 °C)
Freeze only once.	
Stability in CSF:[13]	3 hours at 15-25 °C
	24 hours at 2-8 °C
	2 months at -20 °C (± 5 °C)
Freeze only once.	

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 plasma and CSF

Test definition

Reporting time	10 min		
Wavelength (sub/main)	700/660 nm		
Reagent pipetting		Diluent (H_2O)	
R1	94 µL	15 µL	
R3	19 µL	15 µL	
Sample volumes	*Sample*	*Sample dilution*	
		Sample	*Diluent (NaCl)*
Normal	1.5 µL	-	-
Decreased	1.5 µL	10 µL	90 µL
Increased	1.5 µL	-	-

For further information about the assay test definitions refer to the application parameters setting screen of the corresponding analyzer and assay.

Calibration

Application for plasma

Calibrators	S1: H_2O
	S2: C.f.a.s.
Calibration mode	Linear
Calibration frequency	Automatic full calibration - after reagent lot change Full calibration - as required following quality control procedures

Application for CSF (ACN 20790)

Transfer of calibration from plasma application (ACN 20791)

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

Traceability: This method has been standardized against a primary standard based on NIST-traceable materials.

Quality control

For quality control, use control materials as listed in the "Order information" section. In addition, other suitable control material can be used.

Plasma:	PreciControl ClinChem Multi 1, PreciControl ClinChem Multi 2
CSF:	Quantitative CSF controls are recommended for routine quality control.

The control intervals and limits should be adapted to each laboratory's individual requirements. It is recommended to perform quality control always after lot calibration and subsequently at least every 12 weeks.

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

cobas c systems automatically calculate the analyte concentration of each sample in the unit mmol/L (mg/dL, mg/L).

Conversion factors:	mmol/L x 9.009 = mg/dL
	mmol/L x 90.09 = mg/L

Limitations - interference

Criterion: Recovery within ± 0.22 mmol/L of initial values of samples ≤ 2.2 mmol/L and ± 10 % for samples > 2.2 mmol/L.

Plasma

Icterus:[14] No significant interference up to an I index of 28 for conjugated and 60 for unconjugated bilirubin (approximate conjugated bilirubin concentration: 479 µmol/L or 28 mg/dL; approximate unconjugated bilirubin concentration: 1026 µmol/L or 60 mg/dL).

Hemolysis:[14] No significant interference up to an H index of 1000 (approximate hemoglobin concentration: 621 µmol/L or 1000 mg/dL).

Lipemia (Intralipid):[14] No significant interference up to an L index of 1500. There is poor correlation between the L index (corresponds to turbidity) and triglycerides concentration.

Highly turbid and grossly lipemic samples may cause Abs. flags.

Drugs: No interference was found at therapeutic concentrations using common drug panels.[15,16]

Acetaminophen intoxications are frequently treated with N-acetylcysteine. N-acetylcysteine at a plasma concentration above 750 mg/L and the acetaminophen metabolite N-acetyl-p-benzoquinone imine (NAPQI) independently may cause falsely low results.

Venipuncture should be performed prior to the administration of Metamizole. Venipuncture immediately after or during the administration of Metamizole may lead to falsely low results. A significant interference may occur at any plasma metamizole concentration.

Calcium dobesilate causes artificially low lactate results at the therapeutic drug level.

Glycolate, a metabolite of ethylene glycol, causes a positive interference which is variable from lot to lot of reagent. Dicynone (Etamsylate) at therapeutic concentrations may lead to false-low results.

In very rare cases, gammopathy, in particular type IgM (Waldenström's macroglobulinemia), may cause unreliable results.[17]

LACT2

Lactate Gen.2

CSF

Icterus: No significant interference up to an I index of 6 for conjugated bilirubin (approximate conjugated bilirubin concentration: 102 µmol/L or 6 mg/dL).

Hemolysis: No significant interference up to an H index of 1000 (approximate hemoglobin concentration: 621 µmol/L or 1000 mg/dL).

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 **cobas c** systems. All special wash programming necessary for avoiding carry-over is available via the **cobas** link. The latest version of the carry-over evasion list can be found with the NaOHD/SMS/SCCS Method Sheet. For further instructions, refer to the operator's manual.

Limits and ranges

Measuring range

0.2-15.5 mmol/L (1.8-140 mg/dL)

Determine samples having higher concentrations via the rerun function. Dilution of samples via the rerun function is a 1:10 dilution. Results from samples diluted using the rerun function are automatically multiplied by a factor of 10.

Lower limits of measurement

Limit of Blank, Limit of Detection and Limit of Quantitation

Limit of Blank	= 0.2 mmol/L (1.8 mg/dL)
Limit of Detection	= 0.2 mmol/L (1.8 mg/dL)
Limit of Quantitation	= 0.2 mmol/L (1.8 mg/dL)

The Limit of Blank, Limit of Detection and Limit of Quantitation were determined in accordance with the CLSI (Clinical and Laboratory Standards Institute) EP17-A2 requirements.

The Limit of Blank is the 95th percentile value from n ≥ 60 measurements of analyte-free samples over several independent series. The Limit of Blank corresponds to the concentration below which analyte-free samples are found with a probability of 95 %.

The Limit of Detection is determined based on the Limit of Blank and the standard deviation of low concentration samples.

The Limit of Detection corresponds to the lowest analyte concentration which can be detected (value above the Limit of Blank with a probability of 95 %).

The Limit of Quantitation is the lowest analyte concentration that can be reproducibly measured with a total error of 20 %. It has been determined using low concentration lactate samples.

Expected values

mmol/L

Plasma:	0.5-2.2 mmol/L	venous[9]
CSF:	0.6-2.1 mmol/L	child (female)[18]
	0.9-2.2 mmol/L	child (male)
	1.01-2.09 mmol/L	adult

mg/dL

Plasma:	4.5-19.8 mg/dL	venous[9]
CSF:	5.4-18.9 mg/dL	child (female)[18]
	8.1-19.8 mg/dL	child (male)
	9.1-18.8 mg/dL	adult

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

Specific performance data

Representative performance data on the analyzers are given below. These data represent the performance of the analytical procedure itself.

Results obtained in individual laboratories may differ due to heterogenous sample materials, aging of analyzer components and mixture of reagents running on the analyzer.

Precision

Precision was determined using human samples and controls in accordance with the CLSI (Clinical and Laboratory Standards Institute) EP05-A3 requirements with repeatability (n = 84) and intermediate precision (2 aliquots per run, 2 runs per day, 21 days). Results for repeatability and intermediate precision were obtained on the **cobas c** 503 analyzer.

Plasma

Repeatability	*Mean mmol/L*	*SD mmol/L*	*CV %*
PCCC1[a)]	1.68	0.0105	0.6
PCCC2[b)]	3.63	0.0153	0.4
Human plasma 1	0.510	0.00876	1.7
Human plasma 2	1.71	0.00964	0.6
Human plasma 3	4.56	0.0227	0.5
Human plasma 4	7.88	0.0351	0.4
Human plasma 5	13.1	0.0617	0.5

Intermediate precision	*Mean mmol/L*	*SD mmol/L*	*CV %*
PCCC1[a)]	1.68	0.0145	0.9
PCCC2[b)]	3.63	0.0239	0.7
Human plasma 1	0.494	0.0103	2.1
Human plasma 2	1.72	0.0138	0.8
Human plasma 3	4.56	0.0239	0.5
Human plasma 4	7.88	0.0375	0.5
Human plasma 5	13.2	0.0748	0.6

a) PreciControl ClinChem Multi 1

b) PreciControl ClinChem Multi 2

CSF

Repeatability	*Mean mmol/L*	*SD mmol/L*	*CV %*
Control 1[c)]	1.82	0.0122	0.7
Control 2[c)]	3.71	0.0204	0.6
Human CSF 1	0.502	0.0113	2.2
Human CSF 2	1.74	0.0128	0.7
Human CSF 3	4.50	0.0401	0.9
Human CSF 4	7.90	0.0385	0.5
Human CSF 5	12.8	0.0664	0.5

Intermediate precision	*Mean mmol/L*	*SD mmol/L*	*CV %*
Control 1[c)]	1.82	0.0160	0.9
Control 2[c)]	3.71	0.0241	0.7
Human CSF 1	0.502	0.0124	2.5
Human CSF 2	1.74	0.0157	0.9
Human CSF 3	4.50	0.0456	1.0
Human CSF 4	7.87	0.0498	0.6
Human CSF 5	12.9	0.0831	0.6

c) commercially available control material

The data obtained on **cobas c** 503 analyzer(s) are representative for **cobas c** 303 analyzer(s) and **cobas c** 703 analyzer(s).

Method comparison

Lactate values for human plasma and human CSF samples obtained on a **cobas c** 503 analyzer (y) were compared with those determined using the corresponding reagent on a **cobas c** 501 analyzer (x).

Plasma

Sample size (n) = 75

Passing/Bablok[19]	Linear regression
y = 1.000x + 0 mmol/L	y = 1.004x - 0.0118 mmol/L
τ = 0.993	r = 1.000

The sample concentrations were between 0.490 and 14.2 mmol/L.

CSF

Sample size (n) = 74

Passing/Bablok[19]	Linear regression
y = 0.993x - 0.008 mmol/L	y = 0.994x - 0.0128 mmol/L
τ = 0.985	r = 1.000

The sample concentrations were between 0.340 and 14.9 mmol/L.

Lactate values for human plasma and human CSF samples obtained on a **cobas c** 303 analyzer (y) were compared with those determined using the corresponding reagent on a **cobas c** 501 analyzer (x).

Plasma

Sample size (n) = 71

Passing/Bablok[19]	Linear regression
y = 1.025x - 0.0427 mmol/L	y = 1.026x - 0.0454 mmol/L
τ = 0.992	r = 1.000

The sample concentrations were between 0.450 and 14.3 mmol/L.

CSF

Sample size (n) = 67

Passing/Bablok[19]	Linear regression
y = 1.012x - 0.00123 mmol/L	y = 1.025x - 0.0249 mmol/L
τ = 0.974	r = 1.000

The sample concentrations were between 0.280 and 14.0 mmol/L.

Lactate values for human plasma and human CSF samples obtained on a **cobas c** 703 analyzer (y) were compared with those determined using the corresponding reagent on a **cobas c** 503 analyzer (x).

Plasma

Sample size (n) = 82

Passing/Bablok[19]	Linear regression
y = 1.000x - 0.0100 mmol/L	y = 0.998x - 0.00472 mmol/L
τ = 0.997	r = 1.000

The sample concentrations were between 0.302 and 14.7 mmol/L.

CSF

Sample size (n) = 67

Passing/Bablok[19]	Linear regression
y = 0.990x - 0.0138 mmol/L	y = 0.996x + 0.0124 mmol/L
τ = 0.960	r = 0.998

The sample concentrations were between 0.314 and 15.0 mmol/L.

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 (for USA: see navifyportal.roche.com for definition of symbols used):

CONTENT	Contents of kit
→	Volume for reconstitution
GTIN	Global Trade Item Number

LACT2

Lactate Gen.2

cobas®

Rx only

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

CE 0123

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