

REF	CONTENT	Analyzer(s) on which <b>cobas c</b> pack(s) can be used
03183700 190	Lactate Gen.2 (100 tests)	System-ID 07 6606 2 COBAS INTEGRA 400 plus COBAS INTEGRA 800
10759350 190	Calibrator f.a.s. (12 × 3 mL)	System-ID 07 3718 6
10759350 360	Calibrator f.a.s. (12 × 3 mL, for USA)	System-ID 07 3718 6
12149435 122	Precinorm U plus (10 × 3 mL)	System-ID 07 7999 7
12149435 160	Precinorm U plus (10 × 3 mL, for USA)	System-ID 07 7999 7
12149443 122	Precipath U plus (10 × 3 mL)	System-ID 07 8000 6
12149443 160	Precipath U plus (10 × 3 mL, for USA)	System-ID 07 8000 6
10171743 122	Precinorm U (20 × 5 mL)	System-ID 07 7997 0
10171735 122	Precinorm U (4 × 5 mL)	System-ID 07 7997 0
10171778 122	Precipath U (20 × 5 mL)	System-ID 07 7998 9
10171760 122	Precipath U (4 × 5 mL)	System-ID 07 7998 9
05117003 190	PreciControl ClinChem Multi 1 (20 × 5 mL)	System-ID 07 7469 3
05947626 190	PreciControl ClinChem Multi 1 (4 × 5 mL)	System-ID 07 7469 3
05947626 160	PreciControl ClinChem Multi 1 (4 × 5 mL, for USA)	System-ID 07 7469 3
05117216 190	PreciControl ClinChem Multi 2 (20 × 5 mL)	System-ID 07 7470 7
05947774 190	PreciControl ClinChem Multi 2 (4 × 5 mL)	System-ID 07 7470 7
05947774 160	PreciControl ClinChem Multi 2 (4 × 5 mL, for USA)	System-ID 07 7470 7

## English

### System information

Test LACT2, test ID 0-606; test LACC2, test ID 0-506.

### Intended use

In vitro test for the quantitative determination of the lactate concentration in human plasma and cerebrospinal fluid on COBAS INTEGRA systems.

### Summary

Anaerobic glycolysis markedly increases blood lactate and causes some increase in pyruvate levels, especially with prolonged exercise. The common cause for increased blood lactate and pyruvate is anoxia resulting from such conditions as shock, pneumonia and congestive heart failure. Lactic acidosis may also occur in renal failure and leukemia. Thiamine deficiency and diabetic ketoacidosis are associated with increased levels of lactate and pyruvate.

Lactate levels in cerebrospinal fluid are increased in bacterial meningitis. Increased CSF levels also occur in hypocapnia, hydrocephalus, brain abscesses, cerebral ischemia and any clinical condition associated with reduced oxygenation of the brain and/or increased intracranial pressure.

Lactate measurements that evaluate the acid-base status are used in the diagnosis and treatment of lactic acidosis (abnormally high acidity in the blood).

In recent years, enzymatic methods for the determination of lactate have gained favor over colorimetric and titrimetric methods. Enzymatic methods are generally simple and provide greater specificity, accuracy, and reproducibility.

The first enzymatic method described for the determination of lactate was based on the transfer of hydrogen from lactate to potassium ferricyanide by lactate dehydrogenase. However, the procedure was cumbersome and did not receive wide acceptance.

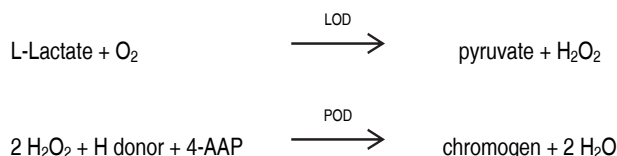
Subsequent methods involved the UV measurement of the formation of NADH. In 1974, Gutmann and Wahlefeld<sup>1</sup> described a lactate procedure that measures the NADH formed by the oxidation of lactate catalyzed by LD, using hydrazine as a trapping agent for pyruvate. A method described by Noll<sup>2</sup> is also based on the catalytic action of LD but includes ALT in the reaction mixture to more rapidly remove the pyruvate formed from the conversion of lactate.

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.<sup>3,4</sup> This method offers longer reagent stability than the previous UV enzymatic methods.

### Test principle

Enzymatic colorimetric method.

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.<sup>3,4</sup>



The intensity of the color formed is directly proportional to the L-lactate concentration. It is determined by measuring the increase in absorbance at 552 nm.

### Reagents - working solutions

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

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

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

### Precautions and warnings

Pay attention to all precautions and warnings listed in Section 1 / Introduction of this Method Manual.

For USA: For prescription use only.

### Reagent handling

Ready for use

### Storage and stability

Shelf life at 2-8 °C	See expiration date on <b>cobas c</b> pack label
COBAS INTEGRA 400 plus system	
On-board in use at 10-15 °C	12 weeks
COBAS INTEGRA 800 system	
On-board in use at 8 °C	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:  
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.

**Do not use serum specimens.**

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.

**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. Thirty 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.<sup>5</sup>
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.<sup>6</sup> 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.

Centrifuge samples containing precipitates before performing the assay.

Stability in <i>plasma (separated)</i> : <sup>7</sup>	8 hours at 15-25 °C
	14 days at 2-8 °C
Stability in <i>plasma (heparinized)</i> : <sup>8</sup>	38 days at -20 °C
Stability in <i>CSF</i> : <sup>9</sup>	3 hours at 15-25 °C
	24 hours at 2-8 °C
	2 months at (-15)-(-25) °C

**Materials provided**

See "Reagents – working solutions" section for reagents.

**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.

**Applications for plasma and CSF****COBAS INTEGRA 400 plus test definition**

Measuring mode	Absorbance
Abs. calculation mode	Endpoint
Reaction mode	R1-S-SR
Reaction direction	Increase
Wavelength A/B	552/659 nm
Calc. first/last	33/49
Unit	mmol/L

**Pipetting parameters**

<i>Plasma, CSF</i>	Diluent (H <sub>2</sub> O)	
R1	125 µL	
Sample	2 µL	20 µL
SR	25 µL	20 µL
Total volume	192 µL	

**COBAS INTEGRA 800 test definition**

Measuring mode	Absorbance
Abs. calculation mode	Endpoint
Reaction mode	R1-S-SR
Reaction direction	Increase
Wavelength A/B	552/659 nm
Calc. first/last	44/70
Unit	mmol/L

**Pipetting parameters**

<i>Plasma, CSF</i>	Diluent (H <sub>2</sub> O)	
R1	125 µL	
Sample	2 µL	20 µL
SR	25 µL	20 µL
Total volume	192 µL	

**Calibration**

Calibrator	Calibrator f.a.s. Use deionized water as zero calibrator.
Calibration mode	Linear regression
Calibration replicate	Duplicate recommended
Calibration interval	Each lot

Traceability: This method has been standardized against a primary standard.

**Quality control**

Reference range	Precinorm U, Precinorm U plus or PreciControl ClinChem Multi 1
Pathological range	Precipath U, Precipath U plus or PreciControl ClinChem Multi 2
Control interval	24 hours recommended
Control sequence	User defined
Control after calibration	Recommended

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**

COBAS INTEGRA analyzers automatically calculate the analyte concentration of each sample. For more details, please refer to Data Analysis in the Online Help (COBAS INTEGRA 400 plus/800 analyzers).

Conversion factor: mmol/L × 9.009 = mg/dL

**Limitations - interference**

Take care in handling lactate specimens. Sweat contains considerable amounts of lactate.

Criterion: Recovery within ± 10 % of initial value.

**Plasma**

Icterus:<sup>10</sup> No significant interference up to an I index of 18 for conjugated bilirubin and 60 for unconjugated bilirubin (approximate conjugated bilirubin concentration: 308 µmol/L or 18 mg/dL; approximate unconjugated bilirubin concentration: 1026 µmol/L or 60 mg/dL).

Hemolysis:<sup>10</sup> No significant interference up to an H index of 1000 (approximate hemoglobin concentration: 621 µmol/L or 1000 mg/dL).

# LACT2

## Lactate Gen.2

Lipemia (Intralipid):<sup>10</sup> No significant interference up to an L index of 2000. There is poor correlation between the L index (corresponds to turbidity) and triglycerides concentration.

Ascorbic acid: No significant interference up to an ascorbic acid level of 1.7 mmol/L (30 mg/dL).

Drugs: No interference was found at therapeutic concentrations using common drug panels.<sup>11,12</sup> Exceptions: calcium dobesilate (e.g. Dexium) causes artificially low lactate results at therapeutic concentrations.

Acetaminophen intoxications are frequently treated with N-Acetylcysteine. N-Acetylcysteine at a plasma concentration above 998 mg/L and the Acetaminophen metabolite N-acetyl-p-benzoquinone imine (NAPQI) independently may cause false-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 plasma Metamizole concentrations above 0.1 mg/mL.

Glycolate, a metabolite of ethylene glycol, causes a positive interference which is variable from lot to lot of reagent.

In very rare cases, gammopathy, in particular type IgM (Waldenström's macroglobulinemia), may cause unreliable results.<sup>13</sup>

The flags 'EP UNSTAB' (endpoint unstable) and 'HIGH ACT' (high activity) are indicators for an extremely high lactate concentration in the sample. These high lactate concentrations can cause false low results due to oxygen depletion. The flag 'EP UNSTAB' can also occur in case of a temperature stressed reagent.

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 INTEGRA analyzers. Refer to the CLEAN Method Sheet for further instructions and for the latest version of the Extra wash cycle list.

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

### Limits and ranges

#### Measuring range for plasma and CSF

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

Lower detection limit of the test:

0.2 mmol/L (1.8 mg/dL)

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 a zero sample (zero sample + 3 SD, repeatability, n = 21).

#### Expected values<sup>5</sup>

Plasma	Venous	0.5-2.2 mmol/L	(4.5-19.8 mg/dL)
	Arterial	0.5-1.6 mmol/L	(4.5-14.4 mg/dL)
CSF	Neonates	1.1-6.7 mmol/L	(10-60 mg/dL)
	3-10 days old	1.1-4.4 mmol/L	(10-40 mg/dL)
	> 10 days old	1.1-2.8 mmol/L	(10-25 mg/dL)
	Adults	1.1-2.4 mmol/L	(10-22 mg/dL)

Roche has not evaluated reference ranges in a pediatric population.

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 COBAS INTEGRA 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 (1 aliquot per run, 1 run per day, 21 days). The following results were obtained:

#### Plasma

Repeatability	Mean		CV
	mmol/L	mg/dL	%
Level 1	1.58	14.2	0.7
Level 2	3.09	27.8	0.8

Intermediate precision	Mean		CV
	mmol/L	mg/dL	%
Level 1	1.57	14.1	1.1
Level 2	3.07	27.7	1.1

#### CSF

Repeatability	Mean		CV
	mmol/L	mg/dL	%
Level 1	1.79	16.1	0.9
Level 2	3.95	35.6	0.6

Intermediate precision	Mean		CV
	mmol/L	mg/dL	%
Level 1	1.55	14.0	1.0
Level 2	3.77	34.0	0.8

### Method comparison

#### Plasma

Lactate values for human plasma samples obtained on a COBAS INTEGRA 700 analyzer with the COBAS INTEGRA Lactate Gen.2 reagent (y) were compared with those determined using the corresponding reagent on a Roche/Hitachi 917 analyzer (x) and with the previous reagent (LACT) on a COBAS INTEGRA 700 analyzer (x).

Sample size (n) = 72

#### Roche/Hitachi 917 analyzer

Passing/Bablok <sup>14</sup>	Linear regression
$y = 1.03x + 0.02$ mmol/L	$y = 1.03x + 0.012$ mmol/L
$r = 0.9879$	$r = 0.9999$
SD (md 95) = 0.041	Sy.x = 0.02

The sample concentrations were between 0.4 and 11.4 mmol/L (3.6 to 103 mg/dL).

#### COBAS INTEGRA 700 analyzer

Passing/Bablok <sup>14</sup>	Linear regression
$y = 1.00x + 0.12$ mmol/L	$y = 0.98x + 0.16$ mmol/L
$r = 0.9804$	$r = 0.9998$
SD (md 95) = 0.10	Sy.x = 0.05

The sample concentrations were between 0.4 and 11.8 mmol/L (3.6 to 106 mg/dL).

#### CSF

Lactate values for human CSF samples obtained on a COBAS INTEGRA 700 analyzer with the COBAS INTEGRA Lactate Gen.2 reagent (y) were compared with those determined using the corresponding reagent on a Roche/Hitachi 917 analyzer (x) and with the previous reagent (LACT) on a COBAS INTEGRA 700 analyzer (x).

Sample size (n) = 47

**Roche/Hitachi 917 analyzer**Passing/Bablok<sup>14</sup>

$$y = 1.00x - 0.002 \text{ mmol/L}$$

$$\tau = 0.9223$$

$$SD \text{ (md 95)} = 0.195$$

Linear regression

$$y = 0.98x + 0.05 \text{ mmol/L}$$

$$r = 0.9969$$

$$Sy.x = 0.09$$

The sample concentrations were between 0.4 and 9.3 mmol/L (3.6 to 83.8 mg/dL).

**COBAS INTEGRA 700 analyzer**Passing/Bablok<sup>14</sup>

$$y = 0.99x + 0.06 \text{ mmol/L}$$

$$\tau = 0.9167$$

$$SD \text{ (md 95)} = 0.215$$

Linear regression

$$y = 0.96x + 0.11 \text{ mmol/L}$$

$$r = 0.9969$$

$$Sy.x = 0.09$$

The sample concentrations were between 0.3 to 9.7 mmol/L (2.7 to 87.4 mg/dL).

**References**

- Gutmann I, Wahlefeld A. Methods of Enzymatic Analysis. 2nd ed. Bergmeyer HU, ed. New York, NY: Academic Press Inc 1974:1464.
- Noll F. Methods of Enzymatic Analysis. 2nd ed. Bergmeyer HU (ed), New York, NY: Academic Press Inc 1974:1475.
- Trinder P. Determination of glucose in blood using glucose oxidase with an alternative oxygen acceptor. Ann Clin Biochem 1969;6:24-27.
- Barhan D, Trinder P. An improved colour reagent for the determination of blood glucose by the oxidase system. Analyst 1972;97:142.
- Tietz NW, ed. Clinical Guide to Laboratory Tests, 3rd ed. Philadelphia PA: WB Saunders Company 1995:382-383.
- Burtis CA, Ashwood ER, (eds.). Tietz Textbook of Clinical Chemistry. 2nd ed. Pa: WB Saunders Co 1994:976.
- Westgard JO, Lahmeyer BL, Birnbaum ML. Clin Chem 1972;18:1334-1338.
- Nelson SR and Kugler KK. Comparison of Lactate Levels in Acid-Treated and Untreated Blood and Spinal Fluid. Biochemical Medicine 1969;2(4):325-332.
- Kleine TO. Nervensysteme. In: Greiling H, Gressner AM, eds. Lehrbuch der Klinischen Chemie und Pathobiochemie Stuttgart: Schattauer 1987;859-893.
- Glick MR, Ryder KW, Jackson SA. Graphical Comparisons of Interferences in Clinical Chemistry Instrumentation. Clin Chem 1986;32:470-475.
- Breuer J. Report on the Symposium "Drug effects in Clinical Chemistry Methods". Eur J Clin Chem Clin Biochem 1996;34:385-386.
- Sonntag O, Scholer A. Drug interference in clinical chemistry: recommendation of drugs and their concentrations to be used in drug interference studies. Ann Clin Biochem 2001;38:376-385.
- Bakker AJ, Mücke M. Gammopathy interference in clinical chemistry assays: mechanisms, detection and prevention. Clin Chem Lab Med 2007;45(9):1240-1243.
- Bablok W, Passing H, Bender R, et al. A general regression procedure for method transformation. Application of linear regression procedures for method comparison studies in clinical chemistry, Part III. J Clin Chem Clin Biochem 1988 Nov;26(11):783-790.

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.

**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

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