LI

cobas®

Lithium

Order information

REF	CONTENT		Analyzer(s) on which **cobas c** pack(s) can be used
04679598 190	Lithium 100 tests	System-ID 07 6934 7	Roche/Hitachi **cobas c** 311, **cobas c** 501/502
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	
10171743 122	Precinorm U (20 x 5 mL)	Code 300	
10171735 122	Precinorm U (4 x 5 mL)	Code 300	
10171778 122	Precipath U (20 x 5 mL)	Code 301	
10171760 122	Precipath U (4 x 5 mL)	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	

English

System information

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

LI: ACN 136

For **cobas c** 502 analyzer:

LI: ACN 8136

Intended use

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

Summary[1,2]

Lithium is widely used in the treatment of manic depressive psychosis. Administered as lithium carbonate, it is completely absorbed by the gastro-intestinal tract; peak serum levels occur 2 to 4 hours after an oral dose. The half life in serum is 48 to 72 hours and it is cleared through the kidneys (excretion parallels that of sodium). Reduced renal function can prolong clearance time. Lithium acts by enhancing the uptake of neurotransmitters, which produces a sedative effect on the central nervous system. Serum lithium concentrations are measured essentially to ensure compliance and to avoid toxicity. Early symptoms of intoxication include apathy, sluggishness, drowsiness, lethargy, speech difficulties, irregular tremors, myoclonic twitchings, muscle weakness and ataxia.

Levels higher than 1.5 mmol/L (12 hours after a dose) indicate a significant risk of intoxication. In the diagnostic laboratory, lithium has traditionally been measured using either flame emission photometry, atomic absorption spectrometry, or ion selective electrodes. These methods require specific and often dedicated instrumentation. This lithium test is a colorimetric method.

Test principle[2]

Colorimetric test.

Lithium present in the sample reacts with a substituted porphyrin compound at an alkaline pH, resulting in a change in absorbance which is directly proportional to the concentration of lithium in the sample.

Reagents - working solutions

R1 Sodium hydroxide: 0.5 mol/L; EDTA: 50 µmol/L; substituted porphyrin: 15 µmol/L; preservative; detergent

R1 is in position B.

Precautions and warnings

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

Disposal of all waste material should be in accordance with local guidelines. Safety data sheet available for professional user on request.

For USA: For prescription use only.

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

Danger

H290	May be corrosive to metals.
H314	Causes severe skin burns and eye damage.

Prevention:

P280	Wear protective gloves/ protective clothing/ eye protection/ face protection.

Response:

P303 + P361 + P353	IF ON SKIN (or hair): Remove/Take off immediately all contaminated clothing. Rinse skin with water/shower.
P304 + P340 + P310	IF INHALED: Remove person to fresh air and keep comfortable for breathing. Immediately call a POISON CENTER or doctor/physician.
P305 + P351 + P338	IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.

Product safety labeling primarily follows EU GHS guidance.

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

Reagent handling

Ready for use

Storage and stability

LI

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

On-board in use and refrigerated on the analyzer: 4 weeks

Specimen collection and preparation[3,4,5]

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

Only the specimens listed below were tested and found acceptable.
Serum.
Plasma: K_2-EDTA and Na-heparin plasma.

Do not use lithium heparinized plasma.

The specimen should be separated from cells if storage for more than 4 hours is anticipated.

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.

Stability:[4]	1 day at 15-25 °C
	7 days at 2-8 °C
	6 months at (-15)-(-25) °C

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	1-Point	
Reaction time / Assay points	10 / 7	
Wavelength (sub/main)	480/505 nm	
Reaction direction	Decrease	
Unit	mmol/L (mg/dL)	
Reagent pipetting		Diluent
R1	100 µL	-
R2	-	-

Sample volumes	*Sample*	*Sample dilution*	
		Sample	Diluent (H_2O)
Normal	4 µL	5 µL	100 µL
Decreased	2 µL	5 µL	100 µL
Increased	4 µL	5 µL	100 µL

cobas c 501 **test definition**

Assay type	1-Point	
Reaction time / Assay points	10 / 11	
Wavelength (sub/main)	480/505 nm	
Reaction direction	Decrease	
Unit	mmol/L (mg/dL)	
Reagent pipetting		Diluent
R1	100 µL	-
R2	-	-

Sample volumes	*Sample*	*Sample dilution*	
		Sample	Diluent (H_2O)
Normal	4 µL	5 µL	100 µL
Decreased	2 µL	5 µL	100 µL
Increased	4 µL	5 µL	100 µL

cobas c 502 **test definition**

Assay type	1-Point	
Reaction time / Assay points	10 / 11	
Wavelength (sub/main)	480/505 nm	
Reaction direction	Decrease	
Unit	mmol/L (mg/dL)	
Reagent pipetting		Diluent
R1	100 µL	-
R2	-	-

Sample volumes	*Sample*	*Sample dilution*	
		Sample	Diluent (H_2O)
Normal	4 µL	5 µL	100 µL
Decreased	2 µL	5 µL	100 µL
Increased	4 µL	10 µL	100 µL

Calibration

Calibrators	S1: H_2O
	S2: C.f.a.s.
Calibration mode	Linear
Calibration frequency	2-point calibration • after 7 days on-board • after **cobas c** pack change • after reagent lot change • as required following quality control procedures

Traceability: The lithium calibrator C.f.a.s. is traceable against AAS.

US only: The lithium calibrator C.f.a.s. is traceable against SRM 956b.

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 concentration of each sample.

Conversion factors:	mmol/L x 0.6941 = mg/dL
	mg/dL x 1.441 = mmol/L

Limitations – interference

Criterion: Recovery within ± 10 % of initial values at therapeutic concentrations.[6]

Icterus:[7] No significant interference up to an I index of 43 for conjugated and 37 for unconjugated bilirubin (approximate conjugated bilirubin concentration: 735 µmol/L or 43 mg/dL and approximate unconjugated bilirubin concentration: 633 µmol/L or 37 mg/dL).

Hemolysis:[7] No significant interference up to an H index of 1000 (approximate hemoglobin concentration: 621 µmol/L or 1000 mg/dL).

Lipemia (Intralipid):[7] No significant interference up to an L index of 2000. 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.[8,9]

Key interferences:

Criterion: Recovery within ± 5 % of initial values at therapeutic concentrations.[8]

NH_4Cl (19.8 µmol/L), NaCl (140 mmol/L), KCl (4 mmol/L),

$CaCl_2$ (2.4 mmol/L), $MgCl_2$ (0.9 mmol/L), $FeCl_3$ (1.04 mg/L),

$Cu(NO_3)_2$ (1.15 mmol/L), $ZnCl_2$ (1.07 mmol/L).

No significant interference was found in the physiological key interference range.

In very rare cases, gammopathy, in particular type IgM (Waldenström's macroglobulinemia), may cause unreliable results.[10]

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-SmpCln1+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 not required.

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

Limits and ranges

Measuring range

0.05-3.00 mmol/L (0.03-2.08 mg/dL)

Determine samples having higher concentrations via the rerun function. Dilution of samples via the rerun function is a 1:2 dilution. Results from samples diluted using the rerun function are automatically multiplied by a factor of 2.

Lower limits of measurement

Limit of Blank (LoB) and Limit of Detection (LoD)

Limit of Blank:	= 0.03 mmol/L (0.02 mg/dL)
Limit of Detection:	= 0.05 mmol/L (0.03 mg/dL)

The Limit of Blank and Limit of Detection were determined in accordance with the CLSI (Clinical and Laboratory Standards Institute) EP17-A 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 %).

Values below the Limit of Detection (< 0.05 mmol/L or 0.03 mg/dL) will not be flagged by the instrument.

Expected values

Lithium[6]	Therapeutic conc.:	0.6-1.2 mmol/L (0.42-0.83 mg/dL)
	Toxic range:	> 2.0 mmol/L (> 1.39 mg/dL)

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. 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:

Repeatability	*Mean*	*SD*	*CV*
	mmol/L (mg/dL)	*mmol/L (mg/dL)*	*%*
Precinorm U	0.77 (0.534)	0.01 (0.007)	1.7
Precipath U	2.38 (1.65)	0.02 (0.01)	1.0
Human serum 1	0.46 (0.319)	0.01 (0.007)	1.9
Human serum 2	1.40 (0.972)	0.02 (0.014)	1.2
Intermediate precision	*Mean*	*SD*	*CV*
	mmol/L (mg/dL)	*mmol/L (mg/dL)*	*%*
Precinorm U	0.79 (0.548)	0.02 (0.014)	2.2
Precipath U	2.42 (1.68)	0.03 (0.02)	1.3
Human serum 1	0.64 (0.444)	0.01 (0.007)	2.3
Human serum 2	1.62 (1.12)	0.03 (0.02)	1.6

Method comparison

Lithium values for human serum samples obtained with the lithium reagent on a Roche/Hitachi **cobas c** 501 analyzer (y) were compared to those determined with the same reagent on a Roche/Hitachi 917 analyzer (x) and with the lithium ion-selective electrode on a COBAS INTEGRA 400 analyzer (x).

x = Roche/Hitachi 917 analyzer, y = **cobas c** *501 analyzer*

Sample size (n) = 50

Passing/Bablok[11]	Linear regression
y = 1.034x - 0.013	y = 1.032x - 0.016
τ = 0.959	r = 0.996

The sample concentrations were between 0.434 and 1.36 mmol/L (0.301 and 0.944 mg/dL).

x = COBAS INTEGRA 400 analyzer, y = **cobas c** *501 analyzer*

Sample size (n) = 78

Passing/Bablok[11]	Linear regression
y = 0.989x + 0.037	y = 0.961x + 0.060
τ = 0.958	r = 0.998

The sample concentrations were between 0.120 and 3.35 mmol/L (0.083 and 2.323 mg/dL).

References

1 Monitoring of Lithium. Tietz Fundamentals of Clinical Chemistry. 5th edition, Edited by CA Burtis, ER Ashwood, WB Saunders Co. 2001;631-632(ISBN 0-7216-8634-6).

2 Rumbelow B and Peake M. Performance of a novel spectrophotometric lithium assay on a routine biochemistry analyser. Ann Clin Biochem 2001;38:684-686.

3 Laborparameter Lithium. MTA Dialog 1 (2005): 29.

4 Use of Anticoagulants in Diagnostic Laboratory Investigations. WHO Publication WHO/DIL/LAB/99.1 Rev. 2. Jan. 2002.

5 Infinity Lithium Liquid Stable Reagent. Thermo Electron Corporation. P/N: PI660040en.02 Revised December 2003.

6 Reference Values for Therapeutic and Toxic Drugs. Tietz Fundamentals of Clinical Chemistry. Fifth Edition, Edited by Carl A. Burtis, Edward R. Ashwood, W.B. Saunders Company, 2001: 1023 (ISBN 0-7216-8634-6).

7 Glick MR, Ryder KW, Jackson SA. Graphical Comparisons of Interferences in Clinical Chemistry Instrumentation. Clin Chem 1986;32:470-475.

8 Breuer J. Report on the Symposium "Drug effects in Clinical Chemistry Methods". Eur J Clin Chem Clin Biochem 1996;34:385-386.

9 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.

10 Bakker AJ, Mücke M. Gammopathy interference in clinical chemistry assays: mechanisms, detection and prevention. Clin Chem Lab Med 2007;45(9):1240-1243.

11 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

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.

CE

Roche Diagnostics GmbH, Sandhofer Strasse 116, D-68305 Mannheim
www.roche.com

Distribution in USA by:
Roche Diagnostics, Indianapolis, IN
US Customer Technical Support 1-800-428-2336