

REF	CONTENT	Analyzer(s) on which cobas c pack(s) can be used
04498577 190	Cholinesterase Gen.2 200 tests	System-ID 07 6842 1 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
04489357 190	Diluent NaCl 9 % (50 mL)	System-ID 07 6869 3

English**System information**

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

CHE2: ACN 510

For **cobas c** 502 analyzer:

CHE2: ACN 8510

Intended use

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

Summary^{1,2,3}

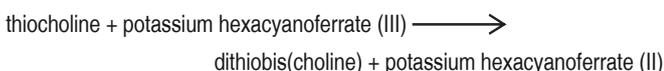
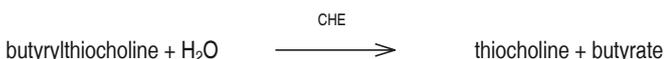
Cholinesterase (pseudocholinesterase or cholinesterase II) is found in the liver, pancreas, heart, serum and in the white matter of the brain. This enzyme must not be confused with acetylcholinesterase from erythrocytes (EC 3.1.1.7), which is also referred to as cholinesterase I.

The biological function of cholinesterase is unknown. Serum cholinesterase serves as an indicator of possible insecticide poisoning. It is measured as an index of liver function. In preoperative screening, cholinesterase is used to detect patients with atypical forms of the enzyme and hence avoid prolonged apnea caused by slow elimination of muscle relaxants.

Depressed cholinesterase levels are found in cases of intoxication with organophosphorus compounds and in hepatitis, cirrhosis, myocardial infarction, acute infections and atypical phenotypes of the enzyme. This assay is based on the method published by Schmidt et al.³

Test principle³

Colorimetric assay



Cholinesterase catalyzes the hydrolysis of butyrylthiocholine to thiocholine and butyrate. Thiocholine instantaneously reduces the yellow hexacyanoferrate (III) to the almost colorless hexacyanoferrate (II). This decrease in color can be measured photometrically.

Reagents - working solutions

R1 Pyrophosphate buffer: 92 mmol/L, pH 7.7; potassium hexacyanoferrate (III): 2.4 mmol/L

R3 GOOD's buffer: 10 mmol/L, pH 4.0; butyrylthiocholine: 46 mmol/L; stabilizers

R1 is in position B and R3 is in position C.

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.

Reagent handling

Ready for use

Storage and stability**CHE2**

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

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 preparation⁴

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 and K₂-EDTA plasma

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: ^{2,4,5}	6 hours at 15-25 °C
	7 days at 2-8 °C
	1 year at -20 °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	Rate A		
Reaction time / Assay points	10 / 29-40		
Wavelength (sub/main)	700/415 nm		
Reaction direction	Decrease		
Units	U/L (µkat/L, kU/L)		
Reagent pipetting	Diluent (H ₂ O)		
R1	120 µL	–	–
R3	24 µL	–	–
<i>Sample volumes</i>	<i>Sample</i>	<i>Sample dilution</i>	
		<i>Sample</i>	<i>Diluent (NaCl)</i>
Normal	2 µL	–	–
Decreased	10 µL	15 µL	135 µL
Increased	2 µL	–	–

cobas c 501 test definition

Assay type	Rate A		
Reaction time / Assay points	10 / 44-54		
Wavelength (sub/main)	700/415 nm		
Reaction direction	Decrease		
Units	U/L (µkat/L, kU/L)		
Reagent pipetting	Diluent (H ₂ O)		
R1	120 µL	–	–
R3	24 µL	–	–
<i>Sample volumes</i>	<i>Sample</i>	<i>Sample dilution</i>	
		<i>Sample</i>	<i>Diluent (NaCl)</i>
Normal	2 µL	–	–
Decreased	10 µL	15 µL	135 µL

Increased	2 µL	–	–
-----------	------	---	---

cobas c 502 test definition

Assay type	Rate A		
Reaction time / Assay points	10 / 44-54		
Wavelength (sub/main)	700/415 nm		
Reaction direction	Decrease		
Units	U/L (µkat/L, kU/L)		
Reagent pipetting	Diluent (H ₂ O)		
R1	120 µL	–	–
R3	24 µL	–	–

<i>Sample volumes</i>	<i>Sample</i>	<i>Sample dilution</i>	
		<i>Sample</i>	<i>Diluent (NaCl)</i>
Normal	2 µL	–	–
Decreased	10 µL	15 µL	135 µL
Increased	4 µL	–	–

Calibration

Calibrators	S1: H ₂ O S2: C.f.a.s.
Calibration mode	Linear
Calibration frequency	2-point calibration <ul style="list-style-type: none"> • after reagent lot change • as required following quality control procedures

Traceability: This test has been standardized against a reference method using a manual application of the butyrylthiocholine/hexacyanoferrate (III) method on a manual photometer and the published molar absorptivity ϵ of hexacyanoferrate (III).³

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.

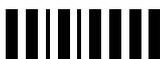
Conversion factors:	U/L x 0.0167 = µkat/L
	µkat/L x 60 = U/L
	U/L x 0.001 = kU/L
	µkat/L x 0.06 = kU/L

Limitations - interference

Criterion: Recovery within $\pm 10\%$ of initial values at a cholinesterase activity of 5000 U/L (83.5 µkat/L).

Icterus:⁶ 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:⁶ No significant interference up to an H index of 700 (approximate hemoglobin concentration: 435 µmol/L or 700 mg/dL).



Lipemia (Intralipid):⁶ No significant interference up to an L index of 1000. 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.^{7,8}

In very rare cases, gammopathy, in particular type IgM (Waldenström's macroglobulinemia), may cause unreliable results.⁹

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/Multiclean/SCCS or 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

100-14000 U/L (1.67-234 μ kat/L)

Determine samples having higher activities 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

Lower detection limit of the test

100 U/L (1.67 μ kat/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^{10,a}

Children, men, women (aged 40 years or more): 5320-12920 U/L (89-215.3 μ kat/L)

Women aged 16-39 years, not pregnant, not taking hormonal contraceptives: 4260-11250 U/L (71-187 μ kat/L)

Women aged 18-41 years, pregnant or taking contraceptives: 3650-9120 U/L (61-152 μ kat/L)

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.

a) Calculated with a temperature conversion factor of 1.52 (25 \rightarrow 37 °C)¹¹

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
	U/L (μ kat/L)	U/L (μ kat/L)	%
Precinorm U	4887 (81.6)	25 (0.4)	0.5
Precipath U	5331 (89.0)	27 (0.5)	0.5
Human serum 1	5916 (98.8)	28 (0.5)	0.5

Human serum 2	7313 (122)	38 (1)	0.5
<i>Intermediate precision</i>	<i>Mean</i>	<i>SD</i>	<i>CV</i>
	U/L (μ kat/L)	U/L (μ kat/L)	%
Precinorm U	4707 (78.6)	49 (0.8)	1.0
Precipath U	4838 (80.8)	45 (0.8)	0.9
Human serum 3	1002 (16.7)	26 (0.4)	2.6
Human serum 4	6683 (112)	74 (1)	1.1

Method comparison

Cholinesterase 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 COBAS INTEGRA 700 analyzer (x).

Sample size (n) = 89

Passing/Bablok ¹²	Linear regression
y = 1.019x - 177 U/L	y = 1.018x - 178 U/L
$\tau = 0.963$	r = 0.999

The sample activities were between 2184 and 12525 U/L (36.5 and 209 μ kat/L).

References

- Moss DW, Henderson AR, Kachmar JF. Enzymes. In: Tietz NW, ed. Fundamentals of Clinical Chemistry, 3rd ed. Philadelphia, PA: WB Saunders 1987;346-421.
- Tietz NW, ed. Clinical Guide to Laboratory Tests, 3rd ed. Philadelphia PA: WB Saunders Company 1995;132-133.
- Schmidt E, et al. Proposal of Standard Methods for the Determination of Enzyme Catalytic Concentrations in Serum and Plasma at 37°C. Eur J Clin Chem Clin Biochem 1992;30:163-170.
- Use of Anticoagulants in Diagnostic Laboratory Investigations. WHO Publication WHO/DIL/LAB/99.1 Rev. 2. Jan. 2002.
- Huizenga JR, van der Belt K, Gips CH. The Effect of Storage at Different Temperatures on Cholinesterase Activity in Human Serum. J Clin Chem Clin Biochem 1985;24:283-385.
- 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.
- den Blaauwen DH, Poppe WA, Tritschler W. Cholinesterase (EC 3.1.1.8) mit Butyrylthiocholiniodid als Substrat:Referenzwerte in Abhängigkeit von Alter und Geschlecht unter Berücksichtigung hormonaler Einflüsse und Schwangerschaft. J Clin Chem Clin Biochem 1983;21:381-386.
- Zawta B, Klein G, Bablok W. Temperature Conversion in Clinical Enzymology? Klin Lab 1994;40:33-42.
- 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.



CHE2

Cholinesterase Gen.2



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.

	Contents of kit
	Volume after reconstitution or mixing

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.

COBAS, COBAS C, COBAS INTEGRA, PRECINORM, PRECIPATH and PRECICONTROL are trademarks of Roche.

All other product names and trademarks are the property of their respective owners.

Significant additions or changes are indicated by a change bar in the margin.

© 2013, Roche Diagnostics



 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

