CKL

Creatine Kinase

cobas®

Order information

REF	CONTENT		Analyzer(s) on which **cobas c** pack(s) can be used
04524977 190	Creatine Kinase 200 tests	System-ID 07 5923 6	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	
11447378 122	Precinorm CK-MB (4 x 3 mL)	Code 320	
04358210 190	Precipath CK-MB (4 x 3 mL, not available in the USA)	Code 356	
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:

CKL: ACN 057

For **cobas c** 502 analyzer:

CK: ACN 8057

Intended use

In vitro test for the quantitative determination of creatine kinase (CK) in human serum and plasma on Roche/Hitachi **cobas c** systems.

Summary[1,2,3,4,5,6]

The CK enzyme is a dimer composed of subunits derived from either muscle (M) or brain (B). Three isoenzymes have been identified: MM, MB, and BB. Normal serum CK is predominantly the CK-MM isoenzyme. Elevated CK-serum levels are found in skeletal muscle disease, particularly muscular dystrophy. The CK-MB fraction is found primarily in myocardial tissue and its presence is generally detected within the 48-hour period following the onset of a myocardial infarction. The use of total CK and CK-MB in the diagnosis of myocardial infarction is the most important single application of CK measurement in clinical chemistry. Serum CK activity is also increased after cerebral ischemia, acute cerebrovascular disease, and head injury.

Standardized methods for the determination of CK using the “reverse reaction” and activation by NAC were recommended by the German Society for Clinical Chemistry (DGKC) and the International Federation of Clinical Chemistry (IFCC) in 1977 and 1989 respectively. This assay follows the recommendations of the IFCC and DGKC, but was optimized for performance and stability.

Test principle

UV-test

$$\text{Creatine phosphate} + \text{ADP} \xrightarrow{\text{CK}} \text{creatine} + \text{ATP}$$

$$\text{ATP} + \text{D-glucose} \xrightarrow{\text{HK}} \text{ADP} + \text{G6P}$$

$$\text{G6P} + \text{NADP}^+ \xrightarrow{\text{G6PDH}} \text{D-6-phosphogluconate} + \text{NADPH} + \text{H}^+$$

The rate of the NADPH formation is directly proportional to the catalytic CK activity. It is determined by measuring the increase in absorbance.

Equimolar quantities of NADPH and ATP are formed at the same rate. The photometrically measured rate of formation of NADPH is directly proportional to the CK activity.

Reagents - working solutions

R1 Imidazole: 58.0 mmol/L, pH 6.00; N-acetylcysteine: 40.0 mmol/L; EDTA: 3.00 mmol/L; AMP: 10.0 mmol/L; diadenosine pentaphosphate: 24.0 µmol/L; $NADP^+$: 9.5 mmol/L; Mg^{2+} : 20.0 mmol/L; D-glucose: 40.0 mmol/L; preservative; stabilizer

R2 EDTA: 3.00 mmol/L, pH 9.1; HK (yeast): ≥ 600 µkat/L; G6PDH (microbial): ≥ 600 µkat/L; ADP: 12.0 mmol/L; creatine phosphate: 180 mmol/L; N-methyldiethanolamine: 69.0 mmol/L; preservative; stabilizer; detergent

R1 is in position B and R2 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.

For USA: For prescription use only.

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

Danger

H360D May damage the unborn child.

Prevention:

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P201	Obtain special instructions before use.
P280	Wear protective gloves/ protective clothing/ eye protection/ face protection.

Response:

P308 + P313	IF exposed or concerned: Get medical advice/attention.

Disposal:

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

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

CKL

Shelf life at 2-8 °C:	See expiration date on **cobas c** pack label.
On-board in use and refrigerated on the analyzer:	8 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 (free from hemolysis). Nonhemolyzed serum is the specimen of choice and also recommended by IFCC.
Plasma (free from hemolysis): Li-heparin plasma

Please note: Differences in the degree of hemolysis resulting from the blood sampling procedure used can lead to deviating results in serum and 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:[7]	2 days at 15-25 °C
	7 days at 2-8 °C
	4 weeks 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	Rate A		
Reaction time / Assay points	10 / 14-28		
Wavelength (sub/main)	546/340 nm		
Reaction direction	Increase		
Units	U/L (µkat/L)		
Reagent pipetting		Diluent (H_2O)	
R1	61 µL	38 µL	
R2	20 µL	–	
Sample volumes	*Sample*	*Sample dilution*	
		Sample	*Diluent (NaCl)*
Normal	3 µL	–	–
Decreased	3 µL	15 µL	135 µL
Increased	3 µL	–	–

cobas c 501 **test definition**

Assay type	Rate A		
Reaction time / Assay points	10 / 21-42		
Wavelength (sub/main)	546/340 nm		
Reaction direction	Increase		
Units	U/L (µkat/L)		
Reagent pipetting		Diluent (H_2O)	
R1	61 µL	38 µL	
R2	20 µL	–	
Sample volumes	*Sample*	*Sample dilution*	
		Sample	*Diluent (NaCl)*
Normal	3 µL	–	–
Decreased	3 µL	15 µL	135 µL
Increased	3 µL	–	–

cobas c 502 **test definition**

Assay type	Rate A		
Reaction time / Assay points	10 / 21-42		
Wavelength (sub/main)	546/340 nm		
Reaction direction	Increase		
Units	U/L (µkat/L)		
Reagent pipetting		Diluent (H_2O)	
R1	61 µL	38 µL	
R2	20 µL	–	
Sample volumes	*Sample*	*Sample dilution*	
		Sample	*Diluent (NaCl)*
Normal	3 µL	–	–
Decreased	3 µL	15 µL	135 µL
Increased	6 µL	–	–

Calibration

Calibrators	S1: H_2O
	S2: C.f.a.s.
Calibration mode	Linear

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Calibration frequency	2-point calibration • after reagent lot change • as required following quality control procedures

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, ε.[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 factor: U/L x 0.0167 = µkat/L

Limitations - interference

Criterion: Recovery within ± 10 % of initial value at a creatine kinase activity of 140 U/L (2.34 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 200 (approximate hemoglobin concentration: 124 µmol/L or 200 mg/dL). The level of interference may be variable depending on the exact content of erythrocytes.

Lipemia (Intralipid):[8] No significant interference up to an L index of 1000. There is poor correlation between the L index (corresponds to turbidity) and triglycerides concentration. Highly lipemic specimens (L index > 1000) may cause high absorbance flagging. Choose diluted sample treatment for automatic rerun.

Drugs: No interference was found at therapeutic concentrations using common drug panels.[9,10] Exception: Cyanokit (Hydroxocobalamin) may cause interference with results.

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-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

7-2000 U/L (0.12-33.4 µkat/L)

Determine samples having higher activities 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

7 U/L (0.12 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

Reference intervals strongly depend on the patient group and the specific clinical situation.

For healthy people, according to Klein et al.:[12]

CK	µkat/L	U/L
Men	0.65-5.14	39-308
Women	0.43-3.21	26-192

Consensus values:[13]

CK	µkat/L	U/L
Men	< 3.20	< 190
Women	< 2.85	< 170

Consensus values:[13]

CK-MB	µkat/L	U/L
Men/women	< 0.42	< 25

Myocardial infarction: There is a high probability of myocardial damage when the following three conditions are fulfilled:[14]

		µkat/L	U/L
1	CK_{men}	> 3.17	> 190
	CK_{women}	> 2.79	> 167
2	CK-MB	> 0.40	> 24
3	The CK-MB activity accounts for 6-25 % of the total CK-activity.		

According to Tietz:[15]

CK	µkat/L	U/L
Adult males > 19 years	0.33-3.34	20-200
Adult females > 19 years	0.33-3.01	20-180

The reference values according to Klein et al. are based on the 95th percentile of a group of healthy persons (202 men and 217 women) not involved in high-intensity athletic activities.

In order to ensure high sensitivity in the diagnosis of heart diseases the values given by Tietz are recommended. The loss of diagnostic specificity thereby incurred can be compensated for by additionally determining CK-MB and/or troponin T. When myocardial infarction is suspected the diagnostic strategy proposals in the consensus document of European and American cardiologists should in general be followed.[16]

If despite the suspicion of myocardial infarction the values found remain below the stated limits, a fresh infarction may be involved. In such cases, the determinations should be repeated after 4 hours.

CK varies with physical activity level and race in healthy individuals.[15,17]

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*
	U/L (µkat/L)	*U/L (µkat/L)*	*%*
Precinorm U	174 (2.91)	1 (0.02)	0.5

Precipath U	390 (6.51)	2 (0.03)	0.5
Human serum 1	49.1 (0.820)	1.1 (0.018)	2.3
Human serum 2	702 (11.7)	5 (0.1)	0.7
Intermediate precision	*Mean*	*SD*	*CV*
	U/L (µkat/L)	*U/L (µkat/L)*	*%*
Precinorm U	164 (2.74)	3 (0.05)	1.8
Precipath U	350 (5.85)	6 (0.10)	1.8
Human serum 3	90.3 (1.51)	3.0 (0.05)	3.3
Human serum 4	309 (5.16)	8 (0.13)	2.5

Method comparison

Creatine kinase 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).

Sample size (n) = 252

Passing/Bablok[18]	Linear regression
y = 1.000x + 7.618 U/L	y = 0.998x + 6.272 U/L
τ = 0.957	r = 0.997

The sample activities were between 19.0 and 1817 U/L (0.317 and 30.3 µkat/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.

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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