

REF	CONTENT	Analyzer(s) on which cobas c pack(s) can be used
04524977 190	Creatine Kinase (200 tests)	System-ID 07 5923 6 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 CKL, test ID 0-323

Intended use

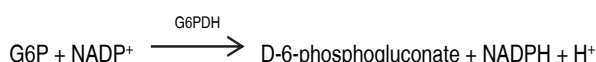
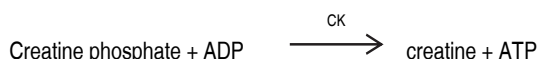
In vitro test for the quantitative determination of the catalytic activity of CK (EC 2.7.3.2; adenosine triphosphate: creatine N-phosphotransferase) in human serum and plasma on COBAS INTEGRA systems.

Summary^{1,2}

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.

Test principle

Method according to the recommendations of the International Federation of Clinical Chemistry (IFCC), the Société Française de Biologie Clinique (SFBC), the Committee on Enzymes of the Scandinavian Society for Clinical Chemistry and Clinical Physiology (SCE), and the Deutsche Gesellschaft für Klinische Chemie (DGKC).^{3,4,5,6}



The rate of the NADPH formation is directly proportional to the catalytic CK activity. It is determined by measuring the increase in absorbance at 340 nm.

Reagents - working solutions

- R1** Imidazole: 58 mmol/L, pH 6.0; N-acetylcysteine: 40 mmol/L; EDTA: 3 mmol/L; AMP: 10 mmol/L; diadenosine pentaphosphate: 24 μmol/L; NADP⁺: 9.5 mmol/L; Mg²⁺: 20 mmol/L; D-glucose: 40 mmol/L; stabilizer
- SR** EDTA: 3 mmol/L, pH 9.1; HK (yeast): ≥ 600 μkat/L; G6PDH (microbial): ≥ 600 μkat/L; ADP: 12 mmol/L; creatine phosphate: 180 mmol/L; N-methyldiethanolamine: 69 mmol/L; sodium azide: 0.09 %; stabilizer; detergent

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.

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



Danger

H360D May damage the unborn child.

Prevention:

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

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

COBAS INTEGRA 400 plus system

On-board in use at 10-15 °C 8 weeks

COBAS INTEGRA 800 system

On-board in use at 8 °C 8 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): Collect serum using standard sampling tubes.
Plasma (free from hemolysis): Li-heparin 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.

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.

Application for serum and plasma

COBAS INTEGRA 400 plus test definition

Measuring mode	Absorbance
Abs. calculation mode	Kinsearch
Reaction mode	R1-S-SR
Reaction direction	Increase
Wavelength A/B	340/629 nm
Calc. first/last	43/60
Unit	U/L

Pipetting parameters

		Diluent (H ₂ O)
R1	61 µL	9 µL
Sample	3 µL	19 µL
SR	20 µL	10 µL
Total volume	122 µL	

COBAS INTEGRA 800 test definition

Measuring mode	Absorbance
Abs. calculation mode	Kinsearch
Reaction mode	R1-S-SR
Reaction direction	Increase

Wavelength A/B	340/629 nm
Calc. first/last	61/91
Unit	U/L

Pipetting parameters

		Diluent (H ₂ O)
R1	61 µL	9 µL
Sample	3 µL	19 µL
SR	20 µL	10 µL
Total volume	122 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 and as required following quality control procedures

Traceability: This method has been standardized manually against the original IFCC formulation.

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

Conversion factor: U/L × 0.0167 = µkat/L

Limitations - interference

Criterion: Recovery within ± 10 % of initial value.

Serum/plasma

Icterus:⁸ No significant interference up to an I index of 15 for conjugated and unconjugated bilirubin (approximate conjugated and unconjugated bilirubin concentration: 255 µmol/L or 15 mg/dL).

Hemolysis:⁸ No significant interference up to an H index of 100 (approximate hemoglobin concentration: 62 µmol/L or 100 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 2000. There is poor correlation between the L index (corresponds to turbidity) and triglycerides concentration. Highly lipemic specimens 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} Exceptions: Calcium dobesilate causes artificially

low CK values at the tested drug level. Hydroxocobalamin (Cyanokit) may cause false-low 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 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

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 a zero sample (zero sample + 3 SD, repeatability, n = 30).

Expected values

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

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

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

Consensus values¹³

CK	Men	< 190 U/L	(< 3.20 µkat/L)
	Women	< 170 U/L	(< 2.85 µkat/L)
CK-MB	Men/women	< 28 U/L	(< 0.42 µkat/L)

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

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

According to Tietz:¹⁵

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

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 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 and intermediate precision (2 aliquots per run, 2 runs per day, 20 days). The following results were obtained:

	Level 1	Level 2
Mean	239 U/L (3.97 µkat/L)	1641 U/L (27.2 µkat/L)
CV repeatability	1.1 %	1.2 %
CV intermediate precision	1.9 %	2.0 %

Method comparison

CK values for human serum and plasma samples obtained on a COBAS INTEGRA 700 analyzer with the COBAS INTEGRA Creatine Kinase reagent (y) were compared with those determined using the commercially available reagents for CK on a COBAS INTEGRA analyzer (x) and an alternative clinical chemistry system (x). Samples were measured in duplicate.

		COBAS INTEGRA analyzer	Alternative system
Sample size	(n)	252	250
Corr. coefficient	(r)	0.998	0.995
	(r _s)	0.998	0.997
Linear regression	y = 1.066x - 3.09 U/L	y = 0.993x - 0.212 U/L	
Passing/Bablok ¹⁸	y = 1.071x - 2.27 U/L	y = 0.985x + 1.85 U/L	

The sample activities were between 5 and 1330 U/L (0.084 to 22.2 µkat/L).

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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.

	Contents of kit
	Volume after reconstitution or mixing
	Global Trade Item Number

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