

CREJ2

Creatinine Jaffé Gen.2 - Compensated Method for Serum and Plasma

cobas®

Substrates

Order information

REF	CONTENT	Analyzer(s) on which cobas c pack(s) can be used
04810716 190	Creatinine Jaffé Gen.2 (700 tests)	System-ID 07 6928 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 CREJ2 (compensated method); test ID 0-445 on COBAS INTEGRA 400 plus systems; test ID 0-245 on COBAS INTEGRA 800 systems

Intended use

In vitro test for the quantitative determination of creatinine in human serum and plasma on COBAS INTEGRA systems.

Summary^{1,2,3,4,5}

Chronic kidney disease is a worldwide problem that carries a substantial risk for cardiovascular morbidity and death. Current guidelines define chronic kidney disease as kidney damage or glomerular filtration rate (GFR) less than 60 mL/min per 1.73 m² for three months or more, regardless of cause.

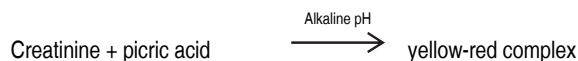
The assay of creatinine in serum or plasma is the most commonly used test to assess renal function. Creatinine is a break-down product of creatine phosphate in muscle, and is usually produced at a fairly constant rate by the body (depending on muscle mass). It is freely filtered by the glomeruli and, under normal conditions, is not re-absorbed by the tubules to any appreciable extent. A small but significant amount is also actively secreted.

Since a rise in blood creatinine is observed only with marked damage of the nephrons, it is not suited to detect early stage kidney disease. A considerably more sensitive test and better estimation of glomerular filtration rate (GFR) is given by the creatinine clearance test based on creatinine's concentration in urine and serum or plasma, and urine flow rate. For this test a precisely timed urine collection (usually 24 hours) and a blood sample are needed. However, since this test is prone to error due to the inconvenient collection of timed urine, mathematical attempts to estimate GFR based only on the creatinine concentration in serum or plasma have been made. Among the various approaches suggested, two have found wide recognition: that of Cockcroft and Gault and that based on the results of the MDRD trial. While the first equation was derived from data obtained with the conventional Jaffé method, a newer version of the second is usable for IDMS-traceable creatinine methods. Both are applicable for adults. In children, the Bedside Schwartz formula should be used.^{6,7,8,9}

In addition to the diagnosis and treatment of renal disease, the monitoring of renal dialysis, creatinine measurements are used for the calculation of the fractional excretion of other urine analytes (e. g., albumin, α-amylase). Numerous methods were described for determining creatinine. Automated assays established in the routine laboratory include the Jaffé alkaline picrate method in various modifications, as well as enzymatic tests.

Test principle^{10,11,12}

This kinetic colorimetric assay is based on the Jaffé method. In alkaline solution, creatinine forms a yellow-red complex with picrate. The rate of dye formation is proportional to the creatinine concentration in the specimen. To correct for non-specific reaction caused by serum/plasma pseudo-creatinine chromogens, including proteins and ketones, the results for serum or plasma are corrected by -18 µmol/L (-0.2 mg/dL).



Reagents - working solutions

R1 Potassium hydroxide: 900 mmol/L; phosphate: 135 mmol/L; pH ≥ 13.5

SR Picric acid: 38 mmol/L; pH 6.5; non reactive buffer

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

H314 Causes severe skin burns and eye damage.

H412 Harmful to aquatic life with long lasting effects.

EUH 001 Explosive when dry

Prevention:

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

Response:

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

Shelf life at 15-25 °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 preparation¹³

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 lipemia): Collect serum using standard sampling tubes.
Plasma (free from lipemia): Li-heparin or 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 in serum/plasma:¹⁴ 7 days at 15-25 °C
7 days at 2-8 °C
3 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 serum and plasma**COBAS INTEGRA 400 plus test definition**

Measuring mode	Absorbance
Abs. calculation mode	Kinetic
Reaction direction	Increase
Wavelength A/B	512/583 nm
Calc. first/last	40/49
Reaction mode	R1-S-SR
Unit	µmol/L

Pipetting parameters

		Diluent (H ₂ O)
R1	13 µL	71 µL

Sample	10 µL	20 µL
SR	17 µL	16 µL
Total volume	147 µL	

COBAS INTEGRA 800 test definition

Measuring mode	Absorbance
Abs. calculation mode	Kinetic
Reaction direction	Increase
Wavelength A/B	512/583 nm
Calc. first/last	55/70
Reaction mode	R1-S-SR
Unit	µmol/L

Pipetting parameters

		Diluent (H ₂ O)
R1	13 µL	41 µL
Sample	10 µL	30 µL
SR	17 µL	36 µL
Total volume	147 µL	

Calibration

Calibrator	Calibrator f.a.s. Use deionized water as zero calibrator.
Calibration mode	Linear regression
Calibration replicate	Duplicate recommended
Calibration interval	COBAS INTEGRA 400 plus analyzers: Each cobas c pack and 7 days, and as required following quality control procedures COBAS INTEGRA 800 analyzers: Each lot and as required following quality control procedures

Traceability: This method has been standardized against ID/MS.^{a)}

For the USA, this method has been standardized against a primary reference material (SRM^{b)} 914 and SRM 967 (ID/MS)).

a) Isotope Dilution Mass Spectrometry

b) Standard Reference Material

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: $\mu\text{mol/L} \times 0.0113 = \text{mg/dL}$

Limitations - interference

Criterion: Recovery in the creatinine decision range for adults ($90 \mu\text{mol/L}$ in serum) within $\pm 10\%$ of initial value.

COBAS INTEGRA 400 plus system:

Hemolysis:¹⁵ No significant interference up to an H index of 800 (approximate hemoglobin concentration: $497 \mu\text{mol/L}$ or 800 mg/dL).

COBAS INTEGRA 800 system:

Hemolysis:¹⁵ No significant interference up to an H index of 400 (approximate hemoglobin concentration: $248 \mu\text{mol/L}$ or 400 mg/dL).

Do not use the COBAS INTEGRA Creatinine Jaffé Gen.2 test when testing for creatinine in hemolyzed samples from neonates, infants or adults with an HbF level of $\geq 60 \text{ mg/dL}$ (COBAS INTEGRA 400 plus system) or $\geq 30 \text{ mg/dL}$ (COBAS INTEGRA 800 system).

COBAS INTEGRA 400 plus/800 systems:

Icterus:¹⁵ No significant interference up to an I index of 5 for conjugated and unconjugated bilirubin (approximate conjugated and unconjugated bilirubin concentration: $85 \mu\text{mol/L}$ or 5 mg/dL).

Lipemia (Intralipid):¹⁵ No significant interference up to an L index of 250. There is poor correlation between the L index (corresponds to turbidity) and triglycerides concentration.

Therapeutic drug interference was tested according to the recommendations of the VDGH⁹. No interferences were found.

Exceptions: Antibiotics containing cephalosporin lead to significant false-positive values.^{16,17} Hydroxocobalamin (Cyanokit) may cause artificially low results.

The presence of ketone bodies can cause artificially high results in serum and plasma.

In very rare cases, gammopathy, in particular type IgM (Waldenström's macroglobulinemia), may cause unreliable results.¹⁸

Values $< 0.2 \text{ mg/dL}$ ($< 18 \mu\text{mol/L}$) or negative results are reported in rare cases in children < 3 years and elderly patients. In such cases use the Creatinine plus test to assay the sample.

Estimation of the Glomerular Filtration Rate (GFR) on the basis of the Schwartz Formula can lead to an overestimation.¹⁹

For diagnostic purposes, the results should always be assessed in conjunction with the patient's medical history, clinical examination and other findings.

c) Verband der Diagnostica und Diagnostica Geräte Hersteller. Refer to section A of the Method Manual for a list of drugs tested and their concentrations.

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

$18\text{--}1300 \mu\text{mol/L}$ ($0.2\text{--}14.7 \text{ mg/dL}$)

The measuring range in the instrument settings is defined as $36\text{--}1318 \mu\text{mol/L}$ ($0.4\text{--}14.9 \text{ mg/dL}$) due to the compensation offset of $18 \mu\text{mol/L}$ (0.2 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:
 $18 \mu\text{mol/L}$ (0.2 mg/dL)

The lower detection limit represents the lowest measurable analyte level that can be distinguished from zero. It is calculated on the basis of precision studies with human sera (repeatability, $n = 10$).

Expected values

Adults²⁰

Females	$44\text{--}80 \mu\text{mol/L}$	($0.50\text{--}0.90 \text{ mg/dL}$)
Males	$62\text{--}106 \mu\text{mol/L}$	($0.70\text{--}1.20 \text{ mg/dL}$)

Children²¹

Neonates (premature)	$25\text{--}91 \mu\text{mol/L}$	($0.29\text{--}1.04 \text{ mg/dL}$)
Neonates (full term)	$21\text{--}75 \mu\text{mol/L}$	($0.24\text{--}0.85 \text{ mg/dL}$)
2-12 m	$15\text{--}37 \mu\text{mol/L}$	($0.17\text{--}0.42 \text{ mg/dL}$)
1-< 3 y	$21\text{--}36 \mu\text{mol/L}$	($0.24\text{--}0.41 \text{ mg/dL}$)
3-< 5 y	$27\text{--}42 \mu\text{mol/L}$	($0.31\text{--}0.47 \text{ mg/dL}$)
5-< 7 y	$28\text{--}52 \mu\text{mol/L}$	($0.32\text{--}0.59 \text{ mg/dL}$)
7-< 9 y	$35\text{--}53 \mu\text{mol/L}$	($0.40\text{--}0.60 \text{ mg/dL}$)
9-< 11 y	$34\text{--}65 \mu\text{mol/L}$	($0.39\text{--}0.73 \text{ mg/dL}$)
11-< 13 y	$46\text{--}70 \mu\text{mol/L}$	($0.53\text{--}0.79 \text{ mg/dL}$)
13-< 15 y	$50\text{--}77 \mu\text{mol/L}$	($0.57\text{--}0.87 \text{ mg/dL}$)

Creatinine clearance for adults^{22,23} $71\text{--}151 \text{ mL/min}$

Refer to reference 19 for a prospective study on creatinine clearance in children.

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 (3 aliquots per run, 1 run per day, 21 days). The following results were obtained:

	Level 1	Level 2
Mean	$66.0 \mu\text{mol/L}$ (0.746 mg/dL)	$330 \mu\text{mol/L}$ (3.73 mg/dL)
CV repeatability	3.1 %	1.4 %

	Level 1	Level 2
Mean	$65.6 \mu\text{mol/L}$ (0.741 mg/dL)	$323 \mu\text{mol/L}$ (3.65 mg/dL)
CV intermediate precision	2.8 %	1.3 %

Method comparison

Creatinine values for human serum and plasma samples obtained on a COBAS INTEGRA 700 analyzer with the COBAS INTEGRA Creatinine Jaffé Gen.2 (compensated method) reagent (y) were compared with those determined using commercially available reagents for creatinine on a COBAS INTEGRA 700 analyzer (Creatinine plus method) (x). Sample size (n) = 90

COBAS INTEGRA 700 analyzer

Method: enzymatic

Passing/Bablok ²⁴	Linear regression
$y = 1.032x - 2.58 \mu\text{mol/L}$	$y = 1.030x - 1.81 \mu\text{mol/L}$
$r = 0.947$	$r = 0.999$
$SD(\text{md } 95) = 14.4$	$Sy.x = 6.65$

The sample concentrations were between 20.2 and $821 \mu\text{mol/L}$ (0.228 and 9.29 mg/dL).

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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