

**Order information**

REF	CONTENT	Analyzer(s) on which <b>cobas c</b> pack(s) can be used
<b>04810716</b> 190	Creatinine Jaffé Gen.2 (700 tests)	System-ID 07 6928 2 COBAS INTEGRA 400 plus COBAS INTEGRA 800
<b>10759350</b> 190	Calibrator f.a.s. (12 × 3 mL)	System-ID 07 3718 6
<b>10759350</b> 360	Calibrator f.a.s. (12 × 3 mL, for USA)	System-ID 07 3718 6
<b>03121313</b> 122	Precinorm PUC (4 × 3 mL)	System-ID 07 6756 5
<b>03121291</b> 122	Precipath PUC (4 × 3 mL)	System-ID 07 6757 3

**English****System information**

Test CRJ2U; test ID 0-546 on COBAS INTEGRA 400 plus systems; test ID 0-346 on COBAS INTEGRA 800 systems

**Intended use**

In vitro test for the quantitative determination of creatinine in urine on COBAS INTEGRA systems.

**Summary<sup>1,2,3,4,5</sup>**

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 m<sup>2</sup> for three months or more, regardless of cause.

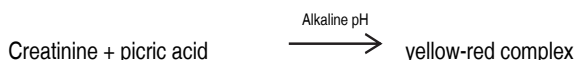
The assay of creatinine in serum or plasma is the most commonly used test to assess renal function. Creatinine is a break-down product of creatine phosphate in muscle, and is usually produced at a fairly constant rate by the body (depending on muscle mass). It is freely filtered by the glomeruli and, 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.<sup>6,7,8,9</sup>

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,  $\alpha$ -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<sup>10,11,12</sup>**

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.

**Reagents - working solutions**

**R1** Potassium hydroxide: 900 mmol/L; phosphate: 135 mmol/L; pH  $\geq 13.5$

**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.

P304 + P340 IF INHALED: Remove person to fresh air and keep comfortable for breathing. 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. 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 preparation<sup>13</sup>**

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

Collect urine without using additives. If urine must be collected with a preservative for other analytes, only hydrochloric acid (14 to 47 mmol/L urine, e.g. 5 mL 10 % HCl or 5 mL 30 % HCl per liter urine) or boric acid (81 mmol/L, e.g. 5 g per liter urine) may be used.

Urine samples are automatically prediluted 1:25 (1 + 24) with water by the instrument.

Stability without preservative: <sup>14</sup>	2 days at 15-25 °C
	6 days at 2-8 °C
	6 months at (-15)-(-25) °C

Stability with preservatives: <sup>15</sup>	3 days at 15-25 °C
	8 days at 2-8 °C
	3 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.

**Applications for urine****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	D-R1-S-SR
Predilution factor	25
Unit	mmol/L

**Pipetting parameters**

		Diluent (H <sub>2</sub> 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	D-R1-S-SR
Predilution factor	25
Unit	mmol/L

**Pipetting parameters**

		Diluent (H <sub>2</sub> 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 <b>cobas c</b> pack, every 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.<sup>a)</sup>

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

a) Isotope Dilution Mass Spectrometry

b) Standard Reference Material

**Quality control**

Reference range	Precinorm PUC
Pathological range	Precipath PUC
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: mmol/L × 11.3 = mg/dL

**Limitations - interference**

Criterion: Recovery in the creatinine decision range for adults (20 mmol/L in urine) within ± 10 % of initial value.

Icterus: No significant interference up to a bilirubin concentration of 855 µmol/L or 50 mg/dL.

Hemolysis: No significant interference up to a hemoglobin concentration of 683 µmol/L or 1100 mg/dL.

Of 12 additional commonly used drugs tested in vitro, none interfered with the assay. Exception: Hydroxocobalamin (Cyanokit) may cause artificially low results.

Glucose < 117 mmol/L (< 2100 mg/dL) and urobilinogen < 676 µmol/L (< 40 mg/dL) do not interfere.

High homogentisic acid concentrations in urine samples lead to false results.

The presence of ketone bodies can cause artificially high results in urine.

In very rare cases, gammopathy, in particular type IgM (Waldenström's macroglobulinemia), may cause unreliable results.<sup>16</sup>

Estimation of the Glomerular Filtration Rate (GFR) on the basis of the Schwartz Formula can lead to an overestimation.<sup>17</sup>

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**

0.027-32.5 mmol/L (0.31-367 mg/dL)

Determine samples having higher concentrations via the rerun function. Dilution of samples via the rerun function is a 1:4 dilution. Results from samples diluted using the rerun function are automatically multiplied by a factor of 4.

**Lower limits of measurement**

Lower detection limit of the test:

0.027 mmol/L (0.31 mg/dL)

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**1st morning urine<sup>18</sup>

Females	2.47-19.2 mmol/L	(28-217 mg/dL)
Males	3.45-22.9 mmol/L	(39-259 mg/dL)

24 h urine<sup>19</sup>

Females	7-14 mmol/24 h	(740-1570 mg/24 h)
Males	9-21 mmol/24 h	(1040-2350 mg/24 h)

Creatinine clearance<sup>19,20</sup> 71-151 mL/min

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	2.16 mmol/L (24.4 mg/dL)	19.1 mmol/L (216 mg/dL)
CV repeatability	1.4 %	0.8 %
CV intermediate precision	2.5 %	1.6 %

**Method comparison**

Creatinine values for human urine samples obtained on a COBAS INTEGRA 700 analyzer with the COBAS INTEGRA Creatinine Jaffé Gen.2 reagent (y) were compared with those determined using the commercially available reagent for creatinine on an alternative manufacturer's clinical chemistry system (x). Samples were measured in duplicate. Sample size (n) represents all replicates. Sample size (n) = 150

**Alternative system**

Passing/Bablok <sup>21</sup>	Linear regression
$y = 1.04x - 0.01$ mmol/L	$y = 1.04x + 0.02$ mmol/L
$r = 0.963$	$r = 0.999$
SD (md 95) = 0.388	$Sy.x = 0.241$

The sample concentrations were between 2.0 and 21.9 mmol/L (22.6 and 247 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



GTIN

Contents of kit

Volume after reconstitution or mixing

Global Trade Item Number

# CREJ2

**Creatinine Jaffé Gen.2 - Urine**

**cobas<sup>®</sup>**  
Substrates

## FOR US CUSTOMERS ONLY: LIMITED WARRANTY

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