CREJ2

Creatinine Jaffé Gen.2

cobas®

Order information

REF		CONTENT		Analyzer(s) on which **cobas c** pack(s) can be used
04810716190	04810716500	Creatinine Jaffé Gen.2 (700 tests)	System ID 07 6928 2	**cobas c** 311, **cobas c** 501/502, COBAS INTEGRA 400 plus

Materials required (but not provided):

		cobas c 311, **cobas c** 501/502	COBAS INTEGRA 400 plus
10759350190	Calibrator f.a.s. (12 x 3 mL)	Code 401	System-ID 07 3718 6
12149435122	Precinorm U plus (10 x 3 mL)	Code 300	System-ID 07 7999 7
12149443122	Precipath U plus (10 x 3 mL)	Code 301	System-ID 07 8000 6
03121313122	Precinorm PUC (4 × 3 mL)	Code 240	System-ID 07 6756 5
03121291122	Precipath PUC (4 × 3 mL)	Code 241	System-ID 07 6757 3
05117003190	PreciControl ClinChem Multi 1 (20 x 5 mL)	Code 391	System-ID 07 7469 3
05947626190	PreciControl ClinChem Multi 1 (4 x 5 mL)	Code 391	System-ID 07 7469 3
05117216190	PreciControl ClinChem Multi 2 (20 x 5 mL)	Code 392	System-ID 07 7470 7
05947774190	PreciControl ClinChem Multi 2 (4 x 5 mL)	Code 392	System-ID 07 7470 7
04489357190	Diluent NaCl 9 % (50 mL)	System-ID 07 6869 3	n.a.

English

Intended use

In vitro test for the quantitative determination of creatinine in human serum, plasma and urine on **cobas c** and COBAS INTEGRA systems.

Summary

Creatinine measurements, performed with this assay, in human serum, plasma and urine are used as an aid in diagnosis and monitoring of renal disease and in monitoring of renal dialysis. Creatinine measurements are also used for the calculation of the fractional excretion of other urine analytes (e. g., albumin, α-amylase).

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 reabsorbed by the tubules to any appreciable extent. A small but significant amount is also actively secreted. Its concentration is thus, inversely related to glomerular filtration rate (GFR).[1,2]

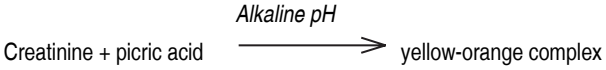
The assay of creatinine in serum or plasma is the most commonly used test to assess renal function. Chronic kidney disease is a worldwide problem that carries a substantial risk for cardiovascular morbidity and death. Current guidelines define chronic kidney disease as kidney damage or decreased glomerular filtration rate (GFR) (less than 60 mL/min per 1.73 m^2) for three months or more.[2,3]

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 (eGFR) based only on the creatinine concentration in serum or plasma have been made.[4] Among the various approaches suggested, three have found wide recognition: the Cockroft and Gault, the Modification of Diet in Renal Disease (MDRD) Study equation and the CKD-EPI (Chronic Kidney Disease Epidemiology) equation. While the Cockcroft and Gault equation was derived from data in which serum creatinine was measured with the conventional Jaffé method, the MDRD study equation measured serum creatinine using the Jaffé method calibrated to an isotope dilution mass spectrometry (IDMS).[5,6] These estimates of GFR are useful during monitoring of renal dialysis.[7,8] In children, the Bedside Schwartz formula should be used.[9,10,11]

In addition to the diagnosis and treatment of renal disease and 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.[2]

Test principle[12,13,14]

This kinetic colorimetric assay is based on the Jaffé method. In alkaline solution, creatinine forms a yellow-orange complex with picrate. The rate of dye formation is proportional to the creatinine concentration in the specimen. The assay uses "rate-blanking" to minimize interference by bilirubin. 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 -26 µmol/L (-0.3 mg/dL) on **cobas c** and by -18 µmol/L (-0.2 mg/dL) on COBAS INTEGRA systems.



Precautions and warnings

For in vitro diagnostic use for health care professionals. Exercise the normal precautions required for handling all laboratory reagents.

Infectious or microbial waste:
Warning: handle waste as potentially biohazardous material. Dispose of waste according to accepted laboratory instructions and procedures.

Environmental hazards:
Apply all relevant local disposal regulations to determine the safe disposal.

Safety data sheet available for professional user on request.

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.

Prevention:

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

Response:

P301 + P330 + P331	IF SWALLOWED: Rinse mouth. Do NOT induce vomiting.
P303 + P361 + P353	IF ON SKIN (or hair): Take off immediately all contaminated clothing. Rinse skin with water.
P304 + P340 + P310	IF INHALED: Remove person to fresh air and keep comfortable for breathing. Immediately call a POISON CENTER/ doctor.
P305 + P351 + P338 + P310	IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing. Immediately call a POISON CENTER/ doctor.

Disposal:

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

Product safety labeling follows EU GHS guidance.

Contact phone: all countries: +49-621-7590

Reagent handling

Ready for use

Specimen collection and preparation[15]

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 K_2-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.

Urine.

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. If stabilizers are added to the sample, the sample index feature must not be used.

Stability in *serum/plasma:*[16]	7 days at 15-25 °C
	7 days at 2-8 °C
	3 months at (-15)-(-25) °C

Freeze only once.

Stability in *urine* (without preservative):[16]	2 days at 15-25 °C
	6 days at 2-8 °C
	6 months at (-15)-(-25) °C

Freeze only once.

Stability in *urine* (with preservative):	3 days at 15-25 °C
	8 days at 2-8 °C
	3 weeks at (-15)-(-25) °C

Freeze only once.

Centrifuge samples containing precipitates before performing the assay.

See the limitations and interferences section for details about possible sample interferences.

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.

Calculation

The systems automatically calculate the analyte concentration of each sample.

Conversion factors:	µmol/L x 0.0113 = mg/dL
	µmol/L x 0.001 = mmol/L
	mmol/L x 11.3 = mg/dL

Expected values

Serum/plasma

Adults[17]

Females	44-80 µmol/L	(0.50-0.90 mg/dL)
Males	62-106 µmol/L	(0.70-1.20 mg/dL)

Children[18]

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

Urine

1st morning urine[17]

Females	2470-19200 µmol/L	(28-217 mg/dL)
Males	3450-22900 µmol/L	(39-259 mg/dL)

24-hour urine[19]

Females	7000-14000 µmol/24 h	(740-1570 mg/24 h)
Males	9000-21000 µmol/24 h	(1040-2350 mg/24 h)

Creatinine clearance[19,20] 71-151 mL/min

Refer to reference for a prospective study on creatinine clearance in children.[21]

Each laboratory should investigate the transferability of the expected values to its own patient population and if necessary determine its own reference ranges.

cobas c systems

System information

Serum/plasma/urine application

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

CREJ2: ACN 690 (Rate blanked, compensated, serum and plasma)

CRJ2U: ACN 691 (Rate blanked, urine)

CREJ2

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SCRE2: ACN 773 (STAT, compensated, serum and plasma, reaction time: 4)

SCR2U: ACN 774 (STAT, urine, reaction time: 4)

For **cobas c** 502 analyzer:

CREJ2: ACN 8690 (Rate blanked, compensated, serum and plasma)

CRJ2U: ACN 8691 (Rate blanked, urine)

SCRE2: ACN 8773 (STAT, compensated, serum and plasma, reaction time: 4)

SCR2U: ACN 8774 (STAT, urine, reaction time: 4)

Reagents - working solutions

R1	Potassium hydroxide: 900 mmol/L; phosphate: 135 mmol/L; pH ≥ 13.5; preservative; stabilizer
R3 (STAT R2)	Picric acid: 38 mmol/L; pH 6.5; non reactive buffer

R1 is in position B and R3 (STAT R2) is in position C.

Storage and stability

Shelf life at 15-25 °C:	See expiration date on **cobas c** pack label.
On-board in use and refrigerated on the analyzer:	8 weeks

Application for serum and plasma

cobas c 311 **test definition**

Assay type	Rate A	
Reaction time / Assay points	10 / 27-37 - 15-23	
	(STAT 4 / 12-19)	
Wavelength (sub/main)	570/505 nm	
Reaction direction	Increase	
Units	µmol/L (mg/dL, mmol/L)	
Reagent pipetting		Diluent (H_2O)
R1	13 µL	77 µL
R3	17 µL	30 µL

Sample volumes	*Sample*	*Sample dilution*	
		Sample	*Diluent (NaCl)*
Normal	10 µL	–	–
Decreased	10 µL	20 µL	80 µL
Increased	10 µL	–	–

Enter the correction value for the non-specific protein reaction as the instrument factor **y = ax + b** for mg/dL or for µmol/L, where **a = 1.0** and **b = -0.3** (mg/dL) or **a = 1.0** and **b = -26** (µmol/L).

cobas c 501/502 **test definition**

Assay type	Rate A	
Reaction time / Assay points	10 / 42-52 - 24-34	
	(STAT 4 / 17-27)	
Wavelength (sub/main)	570/505 nm	
Reaction direction	Increase	
Units	µmol/L (mg/dL, mmol/L)	
Reagent pipetting		Diluent (H_2O)
R1	13 µL	77 µL
R3	17 µL	30 µL

Sample volumes	*Sample*	*Sample dilution*	
		Sample	*Diluent (NaCl)*
Normal	10 µL	–	–
Decreased	10 µL	20 µL	80 µL
Increased	10 µL	–	–

Enter the correction value for the non-specific protein reaction as the instrument factor **y = ax + b** for mg/dL or for µmol/L, where **a = 1.0** and **b = -0.3** (mg/dL) or **a = 1.0** and **b = -26** (µmol/L).

Application for urine

cobas c 311 **test definition**

Assay type	Rate A	
Reaction time / Assay points	10 / 27-37 - 15-23	
	(STAT 4 / 12-19)	
Wavelength (sub/main)	570/505 nm	
Reaction direction	Increase	
Units	µmol/L (mg/dL, mmol/L)	
Reagent pipetting		Diluent (H_2O)
R1	13 µL	77 µL
R3	17 µL	30 µL

Sample volumes	*Sample*	*Sample dilution*	
		Sample	*Diluent (NaCl)*
Normal	10 µL	6 µL	144 µL
Decreased	10 µL	2 µL	180 µL
Increased	10 µL	6 µL	144 µL

cobas c 501 **test definition**

Assay type	Rate A	
Reaction time / Assay points	10 / 42-52 - 24-34	
	(STAT 4 / 17-27)	
Wavelength (sub/main)	570/505 nm	
Reaction direction	Increase	
Units	µmol/L (mg/dL, mmol/L)	
Reagent pipetting		Diluent (H_2O)
R1	13 µL	77 µL
R3	17 µL	30 µL

Sample volumes	*Sample*	*Sample dilution*	
		Sample	*Diluent (NaCl)*
Normal	10 µL	6 µL	144 µL
Decreased	10 µL	2 µL	180 µL
Increased	10 µL	6 µL	144 µL

cobas c 502 **test definition**

Assay type	Rate A	
Reaction time / Assay points	10 / 42-52 - 24-34	
	(STAT 4 / 17-27)	

CREJ2

Creatinine Jaffé Gen.2

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Wavelength (sub/main)	570/505 nm	
Reaction direction	Increase	
Units	µmol/L (mg/dL, mmol/L)	
Reagent pipetting		Diluent (H_2O)
R1	13 µL	77 µL
R3	17 µL	30 µL

Sample volumes	*Sample*	*Sample dilution*	
		Sample	*Diluent (NaCl)*
Normal	10 µL	6 µL	144 µL
Decreased	10 µL	2 µL	180 µL
Increased	10 µL	10 µL	115 µL

Calibration

Calibrators	S1: H_2O
	S2: C.f.a.s.
Calibration mode	Linear
Calibration frequency	2-point calibration
	• after reagent lot change
	• as required following quality control procedures

Calibration interval may be extended based on acceptable verification of calibration by the laboratory.

Traceability: This method has been standardized against ID/MS.[a)]

a) Isotope Dilution Mass Spectrometry

Quality control

Serum/plasma

For quality control, use control materials as listed in the "Order information" section.

In addition, other suitable control material can be used.

Urine

For quality control, use Precinorm PUC and Precipath PUC 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.

Limitations – interference

Criterion: Recovery within ± 10 % of initial value at a creatinine concentration of 80 µmol/L (0.90 mg/dL) in serum/plasma and 2500 µmol/L (28.3 mg/dL) in urine.

Serum/plasma

Icterus (*CREJ2*):[22] No significant interference up to an I index of 5 for conjugated bilirubin and 10 for unconjugated bilirubin (approximate conjugated bilirubin concentration: 86 µmol/L or 5 mg/dL; approximate unconjugated bilirubin concentration: 171 µmol/L or 10 mg/dL).

Icterus (*SCRE2*):[22] No significant interference up to an I index of 2 for conjugated bilirubin and 3 for unconjugated bilirubin (approximate conjugated bilirubin concentration: 34 µmol/L or 2 mg/dL; approximate unconjugated bilirubin concentration: 51 µmol/L or 3 mg/dL).

Hemolysis:[22] No significant interference up to an H index of 1000 (approximate hemoglobin concentration: 621 µmol/L or 1000 mg/dL).

Lipemia (Intralipid):[22] No significant interference up to an L index of 800. There is poor correlation between the L index (corresponds to turbidity) and triglycerides concentration.

Pyruvate: No significant interference from pyruvate up to a concentration of 0.3 mmol/L (2.6 mg/dL).

Glucose: No significant interference from glucose up to a concentration of 25 mmol/L (450 mg/dL).

Ascorbic acid: No significant interference from ascorbic acid up to a concentration of 5 mmol/L (88 mg/dL).

Drugs: No interference was found at therapeutic concentrations using common drug panels.[23,24]

Exception: Antibiotics containing cephalosporin lead to significant false-positive values.[25,26] Cefoxitin causes artificially high creatinine results. Cyanokit (Hydroxocobalamin) may cause interference with results.

Values < 15 µmol/L (< 0.17 mg/dL) or negative results are reported in rare cases in children < 3 years and in elderly patients. In such cases use the Creatinine plus test to assay the sample.

Do not use Creatinine Jaffé for the testing of creatinine in hemolyzed samples from neonates, infants or adults with HbF levels ≥ 60 mg/dL for *CREJ2* applications (≥ 30 mg/dL for *SCRE2* applications).[27] In such cases, use the Creatinine plus test (≤ 600 mg/dL HbF) to assay the sample.

Estimation of the Glomerular Filtration Rate (GFR) on the basis of the Schwartz Formula can lead to an overestimation.[28]

In very rare cases, gammopathy, in particular type IgM (Waldenström's macroglobulinemia), may cause unreliable results.[29]

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

Urine

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

Hemolysis: No significant interference up to a hemoglobin concentration of 621 µmol/L or 1000 mg/dL.

Glucose: No significant interference from glucose up to a concentration of 120 mmol/L (2162 mg/dL).

Urea: No significant interference from urea up to a concentration of 2100 mmol/L (12612 mg/dL).

Urobilinogen: No significant interference from urobilinogen up to a concentration of 676 µmol/L (40 mg/dL).

Drugs: No interference was found at therapeutic concentrations using common drug panels.[24]

Exception: Cyanokit (Hydroxocobalamin) may cause interference with results.

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

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

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 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 required in certain cases.

Where required, special wash/carry-over evasion programming must be implemented prior to reporting results with this test.

Limits and ranges

Measuring range

Serum/plasma

15-2200 µmol/L (0.17-24.9 mg/dL)

The technical limit in the instrument setting is defined as 41-2226 µmol/L (0.463-25.2 mg/dL) due to the compensation factor of 26.

Determine samples having higher concentrations via the rerun function. Dilution of samples via the rerun function is a 1:5 dilution. Results from samples diluted using the rerun function are automatically multiplied by a factor of 5.

Urine

375-55000 µmol/L (4.2-622 mg/dL)

Determine samples having higher concentrations via the rerun function. Dilution of samples via the rerun function is a 1:3.6 dilution. Results from samples diluted using the rerun function are automatically multiplied by a factor of 3.6.

Lower limits of measurement

Limit of Blank and Limit of Detection

Serum/plasma (CREJ2)

Limit of Blank = 15 µmol/L (0.17 mg/dL)

Limit of Detection = 15 µmol/L (0.17 mg/dL)

The Limit of Blank and Limit of Detection were determined in accordance with the CLSI (Clinical and Laboratory Standards Institute) EP17-A requirements.

The Limit of Blank is the 95th percentile value from n ≥ 60 measurements of analyte-free samples over several independent series. The Limit of Blank corresponds to the concentration below which analyte-free samples are found with a probability of 95 %.

The Limit of Detection is determined based on the Limit of Blank and the standard deviation of low concentration samples.

The Limit of Detection corresponds to the lowest analyte concentration which can be detected (value above the Limit of Blank with a probability of 95 %).

Lower detection limit of the test

Serum/plasma (SCRE2)

15 µmol/L (0.17 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 the lowest standard (standard 1 + 3 SD, repeatability, n = 21).

Urine (CRJ2U/SCR2U)

375 µmol/L (4.2 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 the lowest standard (standard 1 + 3 SD, repeatability, n = 21).

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. *Serum/plasma:* repeatability (n = 21) and intermediate precision (3 aliquots per run, 1 run per day, 21 days);
Urine: repeatability (n = 21) and intermediate precision (3 aliquots per run, 1 run per day, 10 days). The following results were obtained on the **cobas c** 501 analyzer:

Serum/plasma (CREJ2)

Repeatability	*Mean*	*SD*	*CV*
	µmol/L (mg/dL)	*µmol/L (mg/dL)*	*%*
Precinorm U	105 (1.19)	2 (0.03)	2.1
Precipath U	360 (4.07)	4 (0.05)	1.1
Human serum 1	206 (2.33)	3 (0.03)	1.2
Human serum 2	422 (4.77)	5 (0.06)	1.3
Intermediate precision	*Mean*	*SD*	*CV*
	µmol/L (mg/dL)	*µmol/L (mg/dL)*	*%*
Precinorm U	101 (1.14)	4 (0.05)	3.5
Precipath U	351 (3.97)	8 (0.09)	2.2
Human serum 3	201 (2.27)	5 (0.06)	2.5
Human serum 4	411 (4.64)	9 (0.10)	2.2

Serum/plasma (SCRE2)

Repeatability	*Mean*	*SD*	*CV*
	µmol/L (mg/dL)	*µmol/L (mg/dL)*	*%*
Precinorm U	106 (1.20)	2 (0.02)	2.2
Precipath U	346 (3.91)	5 (0.06)	1.5
Human serum 1	543 (6.14)	6 (0.07)	1.1
Human serum 2	69 (0.78)	2 (0.02)	3.1
Intermediate precision	*Mean*	*SD*	*CV*
	µmol/L (mg/dL)	*µmol/L (mg/dL)*	*%*
Precinorm U	100 (1.13)	4 (0.05)	4.0
Precipath U	334 (3.77)	10 (0.11)	3.0
Human serum 3	522 (5.90)	12 (0.14)	2.4
Human serum 4	64 (0.72)	3 (0.03)	5.0

Urine (CRJ2U)

Repeatability	*Mean*	*SD*	*CV*
	µmol/L (mg/dL)	*µmol/L (mg/dL)*	*%*
Control Level 1	8083 (91.3)	115 (1.3)	1.4
Control Level 2	15618 (177)	213 (2)	1.4
Human urine 1	19318 (218)	234 (3)	1.2
Human urine 2	7958 (89.9)	130 (1.5)	1.6
Intermediate precision	*Mean*	*SD*	*CV*
	µmol/L (mg/dL)	*µmol/L (mg/dL)*	*%*
Control Level 1	8130 (91.9)	164 (1.9)	2.0
Control Level 2	15533 (176)	251 (3)	1.6
Human urine 3	19353 (219)	385 (4)	2.0
Human urine 4	7932 (89.6)	166 (1.9)	2.1

Urine (SCR2U)

Repeatability	*Mean*	*SD*	*CV*
	µmol/L (mg/dL)	*µmol/L (mg/dL)*	*%*
Control Level 1	6287 (71.0)	82 (0.9)	1.2
Control Level 2	15252 (172)	182 (2)	1.2
Human urine 1	24174 (273)	212 (2)	0.9
Human urine 2	2146 (24.2)	48 (0.5)	2.2
Intermediate precision	*Mean*	*SD*	*CV*
	µmol/L (mg/dL)	*µmol/L (mg/dL)*	*%*
Control Level 1	6943 (78.5)	114 (1.3)	1.6
Control Level 2	15394 (174)	229 (3)	1.5
Human urine 3	24230 (274)	354 (4)	1.5
Human urine 4	2184 (24.7)	54 (0.6)	2.5

The data obtained on **cobas c** 501 analyzer(s) are representative for **cobas c** 311 analyzer(s).

Method comparison

Creatinine values for human serum, plasma and urine samples obtained on a **cobas c** 501 analyzer (y) were compared with those determined on Roche/Hitachi 917/MODULAR P analyzers (x), using the corresponding Roche/Hitachi reagent.

Serum/plasma (CREJ2)

Sample size (n) = 273

CREJ2

Creatinine Jaffé Gen.2

Passing/Bablok[30]	Linear regression
y = 1.000x - 0.653 µmol/L	y = 1.002x - 0.978 µmol/L
τ = 0.973	r = 0.999

The sample concentrations were between 38 and 2178 µmol/L (0.429 and 24.6 mg/dL).

Serum/plasma (SCRE2)

Sample size (n) = 224

Passing/Bablok[30]	Linear regression
y = 1.000x - 14.4 µmol/L	y = 0.996x - 12.2 µmol/L
τ = 0.964	r = 0.999

The sample concentrations were between 66 and 1775 µmol/L (0.746 and 20.1 mg/dL).

Urine (CRJ2U)

Sample size (n) = 223

Passing/Bablok[30]	Linear regression
y = 0.999x + 20.7 µmol/L	y = 0.999x + 41.5 µmol/L
τ = 0.969	r = 0.999

The sample concentrations were between 934 and 50228 µmol/L (10.6 and 568 mg/dL).

Urine (SCR2U)

Sample size (n) = 223

Passing/Bablok[30]	Linear regression
y = 0.999x + 67.8 µmol/L	y = 0.998x + 113 µmol/L
τ = 0.973	r = 0.999

The sample concentrations were between 931 and 48729 µmol/L (10.5 and 551 mg/dL).

The data obtained on **cobas c** 501 analyzer(s) are representative for **cobas c** 311 analyzer(s).

COBAS INTEGRA systems

System information

CREJ2 (compensated method): Test ID 0-445 (serum/plasma)

CRJ2U: Test ID 0-546 (urine)

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.

Storage and stability

Shelf life at 15-25 °C	See expiration date on **cobas c** pack label
On-board in use at 10-15 °C	8 weeks

Application for serum and plasma

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_2O)
R1	13 µL	71 µL
Sample	10 µL	20 µL
SR	17 µL	16 µL
Total volume	147 µL	

Application for urine

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_2O)
R1	13 µL	71 µL
Sample	10 µL	20 µL
SR	17 µL	16 µL
Total volume	147 µL	

Calibration

Calibrator	C.f.a.s. Use deionized water as zero calibrator.
Calibration mode	Linear regression
Calibration replicate	Duplicate recommended
Calibration interval	Each **cobas c** pack, every 7 days, and as required following quality control procedures

Calibration interval may be extended based on acceptable verification of calibration by the laboratory.

Traceability: This method has been standardized against ID/MS.[a)]

a) Isotope Dilution Mass Spectrometry

Quality control

Quality control serum/plasma:

Reference range	Precinorm U plus or PreciControl ClinChem Multi 1
Pathological range	Precipath U plus or PreciControl ClinChem Multi 2

Quality control urine:

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.

Limitations - interference

Serum/plasma

Criterion: Recovery in the creatinine decision range for adults (80 µmol/L in serum) within ± 10 % of initial value.

Hemolysis:[22] No significant interference up to an H index of 800 (approximate hemoglobin concentration: 497 µmol/L or 800 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 ≥ 60 mg/dL.

Icterus:[22] No significant interference up to an I index of 5 for conjugated and unconjugated bilirubin (approximate conjugated and unconjugated bilirubin concentration: 85 µmol/L or 5 mg/dL).

Lipemia (Intralipid):[22] No significant interference up to an L index of 250. There is poor correlation between the L index (corresponds to turbidity) and triglycerides concentration.

Pyruvate: No significant interference from pyruvate up to a concentration of 0.4 mmol/L (3.5 mg/dL).

Ascorbic acid: No significant interference from ascorbic acid up to a concentration of 4 mmol/L (70 mg/dL).

Drugs: No interference was found at therapeutic concentrations using common drug panels.[23,24]
Exceptions: Antibiotics containing cephalosporin lead to significant false-positive values.[26,25] Cefoxitin causes artificially high creatinine results.

Hydroxocobalamin (Cyanokit) may cause artifically 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.[29]

Values < 0.2 mg/dL (< 18 µmol/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.[28]

Urine

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.

Glucose: No significant interference from glucose up to a concentration of 117 mmol/L (2100 mg/dL).

Urobilinogen: No significant interference from urobilinogen up to a concentration of 676 µmol/L (40 mg/dL).

Drugs: No interference was found at therapeutic concentrations using common drug panels.[24] Exception: Hydroxocobalamin (Cyanokit) may cause artificially low results.

Criterion: Recovery within ± 10 % of initial value at a creatinine concentration of 2500 µmol/L (28.3 mg/dL).

Urea: No significant interference from urea up to a concentration of 2100 mmol/L (12612 mg/dL).

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.[29]

Estimation of the Glomerular Filtration Rate (GFR) on the basis of the Schwartz Formula can lead to an overestimation.[28]

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

Serum/plasma

18-1300 µmol/L (0.2-14.7 mg/dL)

The measuring range in the instrument settings is defined as 36-1318 µmol/L (0.4-14.9 mg/dL) due to the compensation offset of 18 µmol/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.

Urine

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

Serum/plasma

Lower detection limit of the test:
18 µmol/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).

Urine

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).

Specific performance data

Representative performance data on the analyzers are given below. Results obtained in individual laboratories may differ.

Precision

Serum/plasma

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 on the COBAS INTEGRA 700 analyzer:

	Level 1	Level 2
Mean	66.0 µmol/L (0.746 mg/dL)	330 µmol/L (3.73 mg/dL)
CV repeatability	3.1 %	1.4 %

	Level 1	Level 2
Mean	65.6 µmol/L (0.741 mg/dL)	323 µmol/L (3.65 mg/dL)
CV intermediate precision	2.8 %	1.3 %

The data obtained on COBAS INTEGRA 700 analyzer(s) are representative for COBAS INTEGRA 400 analyzer(s).

Urine

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 on the COBAS INTEGRA 700 analyzer:

	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 %

The data obtained on COBAS INTEGRA 700 analyzer(s) are representative for COBAS INTEGRA 400 analyzer(s).

Method comparison

Serum/plasma

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[30]	Linear regression
y = 1.032x - 2.58 µmol/L	y = 1.030x - 1.81 µmol/L
τ = 0.947	r = 0.999
SD (md 95) = 14.4	Sy.x = 6.65

The sample concentrations were between 20.2 and 821 µmol/L (0.228 and 9.29 mg/dL).

The data obtained on COBAS INTEGRA 700 analyzer(s) are representative for COBAS INTEGRA 400 analyzer(s).

Urine

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[30]	Linear regression
y = 1.04x - 0.01 mmol/L	y = 1.04x + 0.02 mmol/L
τ = 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).

The data obtained on COBAS INTEGRA 700 analyzer(s) are representative for COBAS INTEGRA 400 analyzer(s).

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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.

Any serious incident that has occurred in relation to the device shall be reported to the manufacturer and the competent authority of the Member State in which the user and/or the patient is established.

Symbols

Roche Diagnostics uses the following symbols and signs in addition to those listed in the ISO 15223-1 standard (for USA: see navifyportal.roche.com for definition of symbols used):

CONTENT	Contents of kit
→	Volume for reconstitution
GTIN	Global Trade Item Number
Rx only	For USA: Caution: Federal law restricts this device to sale by or on the order of a physician.

CE 0123

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