Order information
Creatine Jaffé Gen.2
700 tests Cat. No. 04810716 190 System-ID 07 6928 2
Calibrator f.a.s. (12 x 3 mL) Cat. No. 1079350 190 Code 401
Calibrator f.a.s. (12 x 3 mL, for USA) Cat. No. 1079350 360 Code 401
Precinorm U plus (10 x 3 mL) Cat. No. 12149435 122 Code 300
Precinorm U plus (10 x 3 mL, for USA) Cat. No. 12149435 160 Code 300
Precipath U plus (10 x 3 mL) Cat. No. 12149443 122 Code 301
Precipath U plus (10 x 3 mL, for USA) Cat. No. 12149443 160 Code 301
Precinorm U (20 x 5 mL) Cat. No. 10171743 122 Code 300
Precipath U (20 x 5 mL) Cat. No. 10171778 122 Code 301
Precinorm PUC (4 x 3 mL) Cat. No. 03121313 122 Code 240
Precipath PUC (4 x 3 mL) Cat. No. 03121291 122 Code 241
Diluent NaCl 9 % (50 mL) Cat. No. 04889357 190 System-ID 07 6869 3
Creatine + picric acid Alkaline pH yellow-orange complex
Reagents - working solutions
R1 Potassium hydroxide: 900 mmol/L; phosphate: 135 mmol/L; pH ≥ 13.5; preservative; stabilizer
R2/R3 Picric acid: 38 mmol/L; pH 6.5; non reactive buffer

Precautions and warnings
For in vitro diagnostic use. Exercise the normal precautions required for handling all laboratory reagents. Safety data sheet available for professional user on request. Disposal of all waste material should be in accordance with local guidelines. This kit contains components classified as follows according to the European directive 1999/45/EC.
C – Corrosive. R1 contains potassium hydroxide.
R 1: Explosive when dry. R 4: Forms very sensitive, explosive metallic compounds. R 34: Causes burns.
S 24-25: Avoid contact with skin and eyes. S 26: In case of contact with eyes, rinse immediately with plenty of water and seek medical advice. S 35: This material and its container must be disposed of in a safe way. S 36/37/39: Wear suitable protective clothing, gloves and eye/face protection. S 45: In case of accident or if you feel unwell, seek medical advice immediately (show the label where possible).
Contact phone: all countries: +49-621-7590, USA: +1-800-428-2336
Reagent handling
Ready for use.

Storage and stability
CREJ2
Shell life at 15-25 °C: See expiration date on cobas c pack label.
On-board in use and refrigerated on the analyzer: 8 weeks
Diluent NaCl 9 %
Shell 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. Plasma: Li-heparin and K₂-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.

English
System information
CREJ2: ACN 690 (Rate blanked, compensated, serum and plasma)
CREJ2U: ACN 691 (Rate blanked, urine)
SCREJ2: ACN 773 (STAT, compensated, serum and plasma, reaction time: 4)
SCREJ2U: ACN 774 (STAT, urine, reaction time: 4)

Intended use
In vitro test for the quantitative determination of creatine in human serum, plasma and urine on Roche/Hitachi cobas c systems.

Summary
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 creatine in serum or plasma is the most commonly used test to assess renal function. Creatine 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 creatine 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 Schwartz formula is used.

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, a-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
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 -28 µmol/L (-0.3 mg/dL).
Creatine Jaffé Gen.2

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.

Stability in serum/plasma: 10
7 days at 15-25 °C
7 days at 2-8 °C
3 months at (-15)-(-25) °C

Stability in urine (without preservative): 10
2 days at 15-25 °C
6 days at 2-8 °C
6 months at (-15)-(-25) °C

Stability in urine (with preservative): 11
3 days at 15-25 °C
8 days at 2-8 °C
3 weeks at (-15)-(-25) °C

Centrifuge samples containing precipitates before performing the assay.

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 10/27-37 - 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 (H2O)
R1 13 µL 77 µL
R3 17 µL 30 µL
Sample volumes Sample Sample dilution
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 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 (H2O)
R1 13 µL 77 µL
R3 17 µL 30 µL
Sample volumes Sample Sample dilution
Normal 10 µL 6 µL 144 µL
Decreased 10 µL 2 µL 180 µL
Increased 10 µL 10 µL 115 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 (H2O)
R1 13 µL 77 µL
R3 17 µL 30 µL
Sample volumes Sample Sample dilution
Normal 10 µL 6 µL 144 µL
Decreased 10 µL 2 µL 180 µL
Increased 10 µL 10 µL 115 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 (H2O)
R1 13 µL 77 µL
R3 17 µL 30 µL
Sample volumes Sample Sample dilution
Normal 10 µL 6 µL 144 µL
Decreased 10 µL 2 µL 180 µL
Increased 10 µL 10 µL 115 µL

Calibration
Calibrators S1: H2O
S2: C.f.a.s.
Calibration mode Linear
Calibration frequency 2-point calibration
- after reagent lot change
- and as required following quality control procedures
Traceability: This method has been standardized against IDMS. For the USA, this method has been standardized against a primary reference material (SRM 914).

**Quality control**
For quality control, use control materials as listed in the “Order information” section.
Other suitable control material can be used in addition.
Serum/plasma
For quality control use undiluted serum control material as listed above.
Other suitable control material can be used in addition.

**Urine**
For quality control use Precinorm PUC and Precipath PUC as listed above.
Other suitable control material can be used in addition.
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 limits.
Follow the applicable government regulations and local guidelines for quality control.

**Calculation**
Roche/Hitachi cobas c systems automatically calculate the analyte concentration of each sample.

**Conversion factors:**
\[
\text{µmol/L} \times 0.0113 = \text{mg/dL}
\]
\[
\text{µmol/L} \times 0.001 = \text{mmol/L}
\]

**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): 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 (5 mg/dL) and approximate unconjugated bilirubin concentration: 171 µmol/L (10 mg/dL)).
-Icterus (SCRE2): 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 (2 mg/dL) and approximate unconjugated bilirubin concentration: 51 µmol/L (3 mg/dL)).
-Hemolysis: No significant interference up to an H index of 1000 (approximate hemoglobin concentration: 621 µmol/L (1000 mg/dL)).
-Lipemia (intralipid): No significant interference up to an L index of 800. There is poor correlation between the L index (corresponds to turbidity) and triglycerides concentration.

**Drugs:** No interference was found at therapeutic levels using common drug panels.13

**Exception:** Cefotaxin causes artificially high creatinine results.

**Exception:** Cefamandole (Hydrocortisone) 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 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.15 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.16

In very rare cases gammapathy, in particular type IgM (Waldenström’s macroglobulinemia), may cause unreliable results.

**Urine**
-Icterus: No significant interference up to a conjugated bilirubin concentration of 855 µmol/L (50 mg/dL).
-Hemolysis: No significant interference up to a hemoglobin concentration of 621 µmol/L (1000 mg/dL).
-Glucose < 120 mmol/L (< 2162 mg/dL) and urobilinogen < 676 µmol/L (< 40 mg/dL) do not interfere.

**Drugs:** No interference was found at therapeutic levels using common drug panels.14

Except: Cyanokit (Hydrocortisone) may cause interference with results. High homogentisic acid concentrations in urine samples lead to false results.

**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. Refer to the latest version of the Carry over evasion list found with the NAOH/SMS/Multiclean/SCCS Method Sheet and the operator manual for further instructions.

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)

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 by 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 by the rerun function are automatically multiplied by a factor of 3.6.

**Lower limits of measurement**
-Lower detection limit of the test
-Serum/plasma
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 three standard deviations above that of the lowest standard (standard 1 + 3 SD, repeatability, n = 21).

-Urine
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 three standard deviations above that of the lowest standard (standard 1 + 3 SD, repeatability, n = 21).

**Expected values**
-
**Serum/plasma**
-Adults17

<table>
<thead>
<tr>
<th>Females</th>
<th>44-80 µmol/L</th>
<th>(0.50-0.90 mg/dL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Males</td>
<td>62-106 µmol/L</td>
<td>(0.70-1.20 mg/dL)</td>
</tr>
</tbody>
</table>

-Children18

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

**Urine**
-1st morning urine17

<table>
<thead>
<tr>
<th>Females</th>
<th>2470-19200 µmol/L</th>
<th>(28-217 mg/dL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Males</td>
<td>3450-22900 µmol/L</td>
<td>(39-259 mg/dL)</td>
</tr>
</tbody>
</table>
### 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), intermediate precision** (3 aliquots per run, 1 run per day, 21 days);

Urine: repeatability* (n = 21), intermediate precision** (3 aliquots per run, 1 run per day, 10 days). The following results were obtained:

<table>
<thead>
<tr>
<th>Serum/plasma (CREJ2)</th>
<th>Repeatability*</th>
<th>Mean µmol/L (mg/dL)</th>
<th>SD</th>
<th>CV %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Precinorm U</td>
<td>105 (1.19)</td>
<td>2 (0.03)</td>
<td>2.1</td>
<td></td>
</tr>
<tr>
<td>Precipath U</td>
<td>360 (4.07)</td>
<td>4 (0.05)</td>
<td>1.1</td>
<td></td>
</tr>
<tr>
<td>Human serum 1</td>
<td>206 (2.33)</td>
<td>3 (0.03)</td>
<td>1.2</td>
<td></td>
</tr>
<tr>
<td>Human serum 2</td>
<td>422 (4.77)</td>
<td>5 (0.06)</td>
<td>1.3</td>
<td></td>
</tr>
<tr>
<td>Intermediate precision**</td>
<td>Mean µmol/L (mg/dL)</td>
<td>SD</td>
<td>CV %</td>
<td></td>
</tr>
<tr>
<td>Precinorm U</td>
<td>101 (1.14)</td>
<td>4 (0.05)</td>
<td>3.5</td>
<td></td>
</tr>
<tr>
<td>Precipath U</td>
<td>351 (3.97)</td>
<td>8 (0.09)</td>
<td>2.2</td>
<td></td>
</tr>
<tr>
<td>Human serum 3</td>
<td>201 (2.27)</td>
<td>5 (0.06)</td>
<td>2.5</td>
<td></td>
</tr>
<tr>
<td>Human serum 4</td>
<td>411 (4.64)</td>
<td>9 (0.10)</td>
<td>2.2</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Urine (CRJ2U)</th>
<th>Repeatability*</th>
<th>Mean µmol/L (mg/dL)</th>
<th>SD</th>
<th>CV %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control Level 1</td>
<td>8083 (91.3)</td>
<td>115 (1.3)</td>
<td>1.4</td>
<td></td>
</tr>
<tr>
<td>Control Level 2</td>
<td>15618 (177)</td>
<td>213 (2)</td>
<td>1.4</td>
<td></td>
</tr>
<tr>
<td>Human urine 1</td>
<td>19318 (218)</td>
<td>234 (3)</td>
<td>1.2</td>
<td></td>
</tr>
<tr>
<td>Human urine 2</td>
<td>7968 (89.9)</td>
<td>130 (1.5)</td>
<td>1.6</td>
<td></td>
</tr>
</tbody>
</table>

| Intermediate precision** | Mean µmol/L (mg/dL) | SD | CV % |
| 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)   | 388 (4)             | 2.0 |
| Human urine 4   | 7932 (89.6)   | 166 (1.9)           | 2.1 |

<table>
<thead>
<tr>
<th>Serum/plasma (SCRE2)</th>
<th>Repeatability*</th>
<th>Mean µmol/L (mg/dL)</th>
<th>SD</th>
<th>CV %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Precinorm U</td>
<td>106 (1.20)</td>
<td>2 (0.02)</td>
<td>2.2</td>
<td></td>
</tr>
<tr>
<td>Precipath U</td>
<td>346 (3.91)</td>
<td>5 (0.06)</td>
<td>1.5</td>
<td></td>
</tr>
<tr>
<td>Human serum 1</td>
<td>543 (6.14)</td>
<td>6 (0.07)</td>
<td>1.1</td>
<td></td>
</tr>
<tr>
<td>Human serum 2</td>
<td>69 (0.78)</td>
<td>2 (0.02)</td>
<td>3.1</td>
<td></td>
</tr>
</tbody>
</table>

| Intermediate precision** | Mean µmol/L (mg/dL) | SD | CV % |
| 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 |

### Method comparison

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

<table>
<thead>
<tr>
<th></th>
<th>Sample size (n)</th>
<th>Linear regression</th>
<th>r</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum/plasma (CREJ2)</td>
<td>273</td>
<td>y = 1.000x - 0.65 µmol/L</td>
<td>0.999</td>
</tr>
<tr>
<td></td>
<td>223</td>
<td>y = 0.999x + 20.66 µmol/L</td>
<td>0.999</td>
</tr>
<tr>
<td>Urine (CRJ2U)</td>
<td>224</td>
<td>y = 0.999x + 21.42 µmol/L</td>
<td>0.999</td>
</tr>
<tr>
<td></td>
<td>222</td>
<td>y = 0.999x + 41.55 µmol/L</td>
<td>0.999</td>
</tr>
<tr>
<td>Serum/plasma (SCRE2)</td>
<td>224</td>
<td>y = 0.999x + 21.42 µmol/L</td>
<td>0.999</td>
</tr>
<tr>
<td></td>
<td>222</td>
<td>y = 0.999x + 41.55 µmol/L</td>
<td>0.999</td>
</tr>
<tr>
<td>Urine (SCR2U)</td>
<td>223</td>
<td>y = 0.999x + 21.42 µmol/L</td>
<td>0.999</td>
</tr>
<tr>
<td></td>
<td>222</td>
<td>y = 0.999x + 41.55 µmol/L</td>
<td>0.999</td>
</tr>
</tbody>
</table>

### References


11. Data on file at Roche Diagnostics.


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