

Creatinine PAP FS*

Order Information

| | |
|------------------|---|
| Cat. No. | Kit size |
| 1 1759 99 10 963 |  1800 (R1: 4 x 450, R2: 3 x 600) |
| 1 1759 99 10 962 |  2040 (R1: 6 x 340, R2: 6 x 340) |

Intended Use

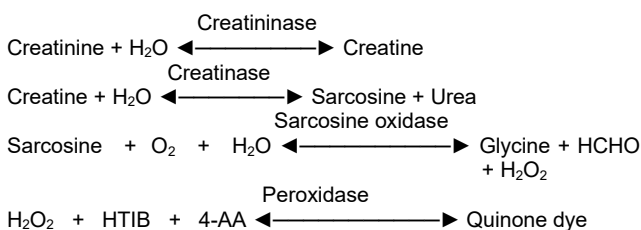
Diagnostic reagent for quantitative in vitro determination of creatinine in human serum, heparin plasma or urine on automated BioMajesty® JCA-BM6010/C.

Summary

Creatinine, a molecule produced by muscle cells, is a byproduct of creatine metabolism and is excreted in urine [1]. Since healthy kidneys consistently filter creatinine through the glomeruli, its blood concentration serves as a marker of kidney function [2]. Creatinine determination is used to evaluate kidney function and detect general kidney damage but is not intended for early-stage detection. Elevated plasma or serum levels indicate impaired kidney function, although age, gender, and muscle mass can influence results [1]. The glomerular filtration rate (GFR) is a more accurate kidney function measure, with a reduced GFR indicating decreased filtration ability [3]. Calculating creatinine clearance, based on plasma, serum, and a 24-hour urine sample, provides a direct kidney filtration assessment, but complex handling may lead to errors [1]. The currently recommended strategy for GFR estimation is based on specific formulas using plasma or serum creatinine values. The latest KDIGO guideline recommends the use of the 2021 CKD-EPI or EKFC formula [4]. This approach is used to screen, diagnose, and classify kidney disease and monitor patients with kidney damage [1,3,4]. Chronic kidney disease (CKD) is one of the most common causes of impaired kidney function. As outlined in the KDIGO guideline CKD is diagnosed when the estimated GFR remains below 60 mL/min/1.73 m² for over three months [4].

Method

Enzymatic, colorimetric test in which creatinine is converted by the use of several enzymes (creatininase, creatinase, and sarcosine oxidase) to produce hydrogen peroxide. In a final reaction in the presence of 4-aminophenazone, the enzyme peroxidase catalyzes the hydrogen peroxide and generates a red quinone dye. The amount of produced red dye measured by the change of absorption at 545 nm is proportional to the amount of creatinine present in the sample. [5, 6]



The absorbance of the produced red dye at 545 nm is proportional to the creatinine concentration in the sample.

Reagents

Components and Concentrations

| | | | |
|------------|---|--------|-------------|
| R1: | Good's buffer | pH 8.1 | 25 mmol/L |
| | Creatinase | | ≥ 30 kU/L |
| | Sarcosine oxidase | | ≥ 10 kU/L |
| | Ascorbate oxidase | | ≥ 2.5 kU/L |
| | Catalase | | ≥ 350 kU/L |
| | HTIB (3-Hydroxy 2,4,6-triiodo benzoic acid) | | 2.3 mmol/L |
| R2: | Good's buffer | pH 8.1 | 25 mmol/L |
| | Creatininase | | ≥ 150 kU/L |
| | Peroxidase | | ≥ 50 kU/L |
| | 4-Aminoantipyrine (4-AA) | | 2 mmol/L |
| | Potassium hexacyanoferrate | | 0.18 mmol/L |

Storage and Stability

Reagents are stable up to the date of expiry indicated on the kit, if stored at 2 – 8°C and contamination is avoided. Do not freeze and protect from light.

The open-vial stability of the reagent is 9 months until expiry date.

Warnings and Precautions

1. Reagent 2 contains sodium azide (0.95 g/L) as preservative. Do not swallow! Avoid contact with skin and mucous membranes.
2. The reagents contain material of biological origin. Handle the product as potentially infectious according to universal precautions and good clinical laboratory practice.
3. High homogenistic acid concentrations in urine samples lead to false results.
4. In very rare cases, samples of patients with gammopathy might give falsified results [7].
5. N-acetylcysteine (NAC), acetaminophen, metamizole and phenindione medication leads to falsely low, eltrombopag medication to falsely low or high results in patient samples.
6. In case of product malfunction or altered appearance that could affect the performance, contact the manufacturer.
7. Any serious incident related to the product must be reported to the manufacturer and the competent authority of the Member State where the user and/or patient is located.
8. Please refer to the safety data sheets (SDS) and take the necessary precautions for the use of laboratory reagents. For diagnostic purposes, the results should always be assessed with the patient's medical history, clinical examinations and other findings.
9. For professional use only.

Waste Management

Refer to local legal requirements for chemical disposal regulations as stated in the relevant SDS to determine the safe disposal.

Warning: Handle waste as potentially biohazardous material. Dispose of waste according to accepted laboratory instructions and procedures.

Reagent Preparation

The reagents are ready to use. The bottles are placed directly into the reagent rotor.

Materials Required

General laboratory equipment

Specimen

Human serum, heparin plasma or urine

Only use suitable tubes or collection containers for specimen collection and preparation.

When using primary tubes, follow the manufacturer's instructions.

Stability in serum/plasma [8]:

| | | |
|----------|----|----------|
| 7 days | at | 4 – 25°C |
| 3 months | at | -20°C |

Stability in urine [8]:

| | | |
|----------|----|-----------|
| 2 days | at | 20 – 25°C |
| 6 days | at | 4 – 8°C |
| 6 months | at | -20°C |

Only freeze once. Discard contaminated specimens.

Calibrators and Controls

DiaSys TruCal U is recommended for calibration. Calibrator values have been made traceable to the NIST (National Institute for Standardization) Standard Reference Material SRM 967 using level 1 and 2 and, therefore, to GC-IDMS (gas chromatography - isotope dilution mass spectrometry). Use DiaSys TruLab N and P or TruLab Urine Level 1 and Level 2 for internal quality control. All target values of the controls are traceable to DiaSys reagent/calibrator system. Quality control must be performed after calibration. Control intervals and limits have to be adapted to the individual requirements of each laboratory. Results must be within the defined ranges. Follow the relevant legal requirements and guidelines. Each laboratory should establish corrective action in case of deviations in control recovery.

| | Cat. No. | Kit Size |
|----------------------|------------------|-----------|
| TruCal U | 5 9100 99 10 063 | 20 x 3 mL |
| | 5 9100 99 10 064 | 6 x 3 mL |
| TruLab N | 5 9000 99 10 062 | 20 x 5 mL |
| | 5 9000 99 10 061 | 6 x 5 mL |
| TruLab P | 5 9050 99 10 062 | 20 x 5 mL |
| | 5 9050 99 10 061 | 6 x 5 mL |
| TruLab Urine Level 1 | 5 9170 99 10 062 | 20 x 5 mL |
| | 5 9170 99 10 061 | 6 x 5 mL |
| TruLab Urine Level 2 | 5 9180 99 10 062 | 20 x 5 mL |
| | 5 9180 99 10 061 | 6 x 5 mL |

Performance Characteristics

Serum/Plasma

Measuring range up to 30 mg/dL, Linearity is given within $\pm 5\%$. In case of higher concentrations re-measure samples after manual dilution with NaCl solution (9 g/L) or use rerun function.

| | |
|-----------------------|------------|
| Limit of detection** | 0.02 mg/dL |
| Onboard stability | 6 weeks |
| Calibration stability | 6 weeks |

| Interference by | Interferences $\leq 10\%$ up to | Analyte concentration [mg/dL] |
|--------------------------|---------------------------------|-------------------------------|
| Ascorbic acid | 27 mg/dL | 0.724 |
| Bilirubin (conjugated) | 18 mg/dL | 1.49 |
| Bilirubin (unconjugated) | 24 mg/dL | 0.735 |
| Creatine | 40 mg/dL | 1.08 |
| Hemolysis | 500 mg/dL | 0.730 |
| Lipemia (triglycerides) | 1700 mg/dL | 1.11 |
| Proline | 12 mg/dL | 1.10 |

For further information on interfering substances, refer to the literature [10-12].

| Precision | | | |
|----------------------|----------|----------|----------|
| Repeatability (n=20) | Sample 1 | Sample 2 | Sample 3 |
| Mean [mg/dL] | 0.654 | 1.24 | 7.13 |
| CV [%] | 0.936 | 1.32 | 0.926 |
| Between day (n=20) | Sample 1 | Sample 2 | Sample 3 |
| Mean [mg/dL] | 0.649 | 1.85 | 6.44 |
| CV [%] | 1.67 | 1.51 | 1.77 |

| Method comparison (n=100) | |
|----------------------------|--|
| Test x | Competitor Creatinine PAP (BioMajesty® JCA-BM6010/C) |
| Test y | DiaSys Creatinine PAP FS (BioMajesty® JCA-BM6010/C) |
| Slope | 0.993 |
| Intercept | 0.039 mg/dL |
| Coefficient of correlation | 0.999 |

Urine

Measuring range up to 300 mg/dL, linearity is given within $\pm 5\%$. In case of higher concentrations re-measure samples after manual dilution with NaCl solution (9 g/L) or use rerun function.

| | |
|-----------------------|-----------|
| Limit of detection** | 0.2 mg/dL |
| Onboard stability | 15 weeks |
| Calibration stability | 15 weeks |

| Precision | | | |
|----------------------|----------|----------|----------|
| Repeatability (n=20) | Sample 1 | Sample 2 | Sample 3 |
| Mean [mg/dL] | 51.3 | 59.2 | 114 |
| CV [%] | 1.29 | 1.42 | 1.36 |
| Between day (n=20) | Sample 1 | Sample 2 | Sample 3 |
| Mean [mg/dL] | 50.6 | 60.2 | 115 |
| CV [%] | 2.31 | 1.79 | 1.50 |

| Method comparison (n=100) | |
|----------------------------|--|
| Test x | Competitor Creatinine PAP (BioMajesty® JCA-BM6010/C) |
| Test y | DiaSys Creatinine PAP FS (BioMajesty® JCA-BM6010/C) |
| Slope | 1.02 |
| Intercept | 0.690 mg/dL |
| Coefficient of correlation | 0.998 |

** lowest measurable concentration which can be distinguished from zero; mean + 3 SD (n = 20) of an analyte free specimen.

Calculation

Creatinine Clearance [mL/min/1.73 m²] [9]

$$= \frac{\text{mg Creatinine} / 100 \text{ mL Urine} \times \text{mL Urine}}{\text{mg Creatinine} / 100 \text{ mL Serum} \times \text{min Urine collection time}}$$

The calculated creatinine clearance refers to the average body surface of an adult (1.73 m²).

Conversion Factor

Creatinine [mg/dL] x 88.4 = Creatinine [μ mol/L]

Creatinine [mg/dL] x 0.0884 = Creatinine [mmol/L]

Reference Range

Serum/Plasma

| | mg/dL | μ mol/L |
|----------------------|-------------|-------------|
| Adults [13] | | |
| Women | 0.51 – 0.95 | 45 – 84 |
| Men | 0.67 – 1.17 | 59 – 104 |
| Children [14] | | |
| 0 – 21 days | 0.26 – 1.01 | 22 – 90 |
| 2 months – < 3 years | 0.15 – 0.39 | 11 – 34 |
| 3 – < 7 years | 0.24 – 0.48 | 21 – 42 |
| 7 – < 11 years | 0.32 – 0.64 | 28 – 57 |
| 11 – < 15 years | 0.42 – 0.81 | 37 – 72 |

Urine

1st Morning urine [13]

| | | |
|-------|----------------|--------------------|
| Women | 29 – 226 mg/dL | 2.55 – 20.0 mmol/L |
| Men | 40 – 278 mg/dL | 3.54 – 24.6 mmol/L |

24h urine [9]

| | | |
|-------|-------------------|-----------------|
| Women | 720 – 1510 mg/24h | 6 – 13 mmol/24h |
| Men | 980 – 2200 mg/24h | 9 – 19 mmol/24h |

Albumin/creatinine ratio (early morning urine) [15]:

< 30 mg/g Creatinine

Creatinine clearance [9]

66.3 – 143 mL/min/1.73 m²

Each laboratory should check if the reference ranges are transferable to its own patient population and determine own reference ranges if necessary.

Literature

1. Thomas L. Clinical Laboratory Diagnostics [Internet]. Prof. Lothar Thomas; 2024 [cited 2024 November 05]. https://www.clinical-laboratory-diagnostics.com/k12.html#_idTextAnchor4288 and https://www.clinical-laboratory-diagnostics.com/k12.html#_idTextAnchor4328.
2. Liu Y, Xu G. Trueness investigation of routine creatinine assays on nine homogeneous systems in Beijing demonstrates an encouraging outcome that meets clinical requirements. Chinese Medical Journal. 2010;123(17):p 2364-2369
3. Boss K, Stolpe S, Müller A, Friebus-Kardash J, et al. Effect of Difference in Serum Creatinine between Jaffe and Enzymatic Methods in Outpatient Kidney Transplant Recipients. Journal of Clinical Medicine. 2024;13(20):6066.
4. Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2024 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. Kidney Int. 2024;105(4S): S117–S314.
5. P Fossati, L Prencipe, G Berti, Enzymic creatinine assay: a new colorimetric method based on hydrogen peroxide measurement., Clinical Chemistry, Volume 29, Issue 8, 1 August 1983, Pages 1494–1496.
6. Lamb E, Newman DJ, Price CP. Kidney Function Tests. In: Burtis CA, Ashwood ER, Bruns DE editors. Tietz Textbook of Clinical Chemistry and Molecular Diagnostics. 4th ed. Elsevier Saunders, St. Louis, Mo., ©2006 p. 799-800.
7. Bakker AJ, Mücke M. Gammopathy interference in clinical chemistry assays: mechanisms, detection and prevention. ClinChemLabMed 2007;45(9):1240-1243.
8. Guder WG, da Fonseca-Wollheim F, Heil W, et al. The Quality of Diagnostic Samples, Deutsche Vereinte Gesellschaft für Klinische Chemie und Laboratoriumsmedizin. 3rd ed; 2010. page 42-3 and 66-7.
9. Junge W, Wilke B, Halabi A, et al. Determination of reference intervals for serum creatinine, creatinine excretion and creatinine clearance with an enzymatic and a modified Jaffé method. Clin Chim Acta. 2004;344:137-148.
10. Young DS. Effects of Drugs on Clinical Laboratory Tests. 5th ed. Volume 1 and 2. Washington, DC: The American Association for Clinical Chemistry Press 2000.
11. Young DS. Effects on Clinical Laboratory Tests - Drugs Disease, Herbs & Natural Products, <https://clinfx.wiley.com/aaccweb/aacc/>, accessed in June 2021. Published by AACC Press and John Wiley and Sons, Inc.
12. Sonntag O, Scholer A. Drug interference in clinical chemistry: recommendation of drugs and their concentrations to be used in drug interference studies. Ann Clin Biochem. 2001 Jul;38:376-85.
13. Mazzachi BC, Peake M, Erhardt V. Reference range and method comparison for enzymatic and Jaffé Creatinine assays in plasma and serum and early morning urine. Clin Lab. 2000;46:53-5.
14. Ceriotti F, Boyd JC, Klein G, et al. Reference intervals for serum creatinine concentrations: assessment of available data for global application. Clinical chemistry. 2008;54(3):559-566.
15. Dati F, Metzmann E. Proteins-Laboratory testing and clinical use. 1st ed. Holzheim: DiaSys Diagnostic Systems; 2005: p. 93.

Additions and/or changes in the document are highlighted in grey. Deletions are communicated via customer info by stating the edition no. of the package insert/instruction for use.



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* Fluid Stable

Creatinine PAP FS

Chemistry code 10 175

Application for serum, plasma and urine samples

This application was set up and evaluated by DiaSys. It is based on the standard equipment at that time and does not apply to any equipment modifications undertaken by unqualified personnel.

| Analytical Conditions | |
|-----------------------|------|
| R1 volume | 80 |
| R2e volume | 0 |
| R2 volume | 40 |
| R1 diluent vol | 0 |
| R2e diluent vol | 0 |
| R2 diluent vol | 0 |
| Sample vol (S) | 2 |
| Sample vol (U) | 2 |
| Reagent 1 mix | weak |
| Reagent 2e mix | weak |
| Reagent 2 mix | weak |
| Reaction time | 10 |

| Sub-analy. Conditions | |
|-----------------------|-------|
| Name | CREAP |
| Digits | 2 |
| M-wave L. | 545 |
| S-wave.L | 694 |
| Analy.mthd. | EPA |
| Calc.mthd. | STD |
| Qualit. judge | No |

| Analysis Test Condition Setting (M) | | |
|-------------------------------------|--------|-----------------------|
| Sample Type | Serum | Urine / Urine control |
| Reac. sample vol. | 2 | 2 |
| Diluent method | No dil | With dil |
| Undil. sample vol. | 0 | 5 |
| Diluent volume | 0 | 45 |
| Diluent position | 0 | 0 |

entered by user

| Endpoint method | |
|-----------------|--------|
| Re.absorb (u) | 9.999 |
| Re. Absorb (d) | -9.999 |

| Calculation Method Setting | |
|----------------------------|-------|
| M-DET.P.l | 0 |
| M-DET.P.m | 41 |
| M-DET.P.n | 42 |
| S-DET.P.p | 17 |
| S-DET.P.r | 18 |
| Check D.P.l. | 0 |
| Limit value | 0.003 |
| Variance | 10 |
| Reac.type | Inc |

| Reaction Rate Method | |
|----------------------|--------|
| Cycle | 2 |
| Factor | 2 |
| E2 corre | Not Do |
| Blank (u) | 9.999 |
| Blank (d) | -9.999 |
| Sample (u) | 9.999 |
| Sample (d) | -9.999 |

| Standards Setting | |
|-------------------|--------|
| FV | # |
| BLK H | 9.999 |
| BLK L | -9.999 |
| STD H | 9.999 |
| STD L | -9.999 |