Creatinine FS*

Diagnostic reagent for quantitative in vitro determination of creatinine in serum, plasma or urine on photometric systems

Order Information

Cat. No.	Kit size					
1 1711 99 10 021	R1	4 x	20 mL	+ R2	1 x	20 mL
	+	1 x	3 mL	Standard		
1 1711 99 10 026	R1	5 x	80 mL	+ R2	1 x	100 mL
1 1711 99 10 023	R1	1 x	800 mL	+ R2	1 x	200 mL
1 1711 99 10 704	R1	8 x	50 mL	+ R2	8 x	12.5 mL
1 1711 99 10 917	R1	8 x	60 mL	+ R2	8 x	15 mL
1 1711 99 90 314	R1	10 x	20 mL	+ R2	2 x	30 mL
1 1700 99 10 030		6 x	3 mL	Standard		

Summary [1,2]

Creatinine is a waste product excreted by the kidneys mainly by glomerular filtration. The concentration of creatinine in plasma of a healthy individual is fairly constant, independent from water intake, exercise and rate of urine production. Therefore, increased plasma creatinine values always indicate decreased excretion, i.e. impaired kidney function. The creatinine clearance enables a quite good estimation of the glomerular filtration rate (GFR) which allows better detection of kidney diseases and monitoring of renal function. For this purpose creatinine is measured simultaneously in serum and urine collected over a defined time period.

Method

Kinetic test without deproteinization according to the Jaffé method

Principle

Creatinine forms a colored orange-red complex in an alkaline picrate solution. The difference in absorbance at fixed times during conversion is proportional to the concentration of creatinine in the sample.

Creatinine + Picric acid ⟶ Creatinine picrate complex

Reagents

Components and Concentrations

R1:	Sodium hydroxide	0.2 mol/L
R2:	Picric acid	20 mmol/L
Standard:		2 mg/dL (177 µmol/L)

Storage Instructions and Reagent Stability

The reagents and the standard are stable up to the end of the indicated month of expiry, if stored at 2 – 25°C and contamination is avoided. Do not freeze the reagents and the standard and protect them from light!

Waste Management

Please refer to local legal requirements.

Reagent Preparation

The standard is ready to use.

Substrate Start

The reagents are ready to use.

Sample Start

Mix 4 parts of R1 + 1 part of R2
(e.g. 20 mL R1 + 5 mL R2) = mono reagent
Stability of mono reagent: 5 hours at 15 – 25°C

Warnings and Precautions

1. Reagent 1: Warning. H290 May be corrosive to metals. H315 Causes skin irritation. H319 Causes serious eye irritation. P234 Keep only in original container. P264 Wash hands and face thoroughly after handling. P280 Wear protective gloves/protective clothing/eye protection. P302+P352 If on skin: Wash with plenty of water/soap. P332+P313 If skin irritation occurs: Get medical advice/attention. P305+P351+P338 If in eyes: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing. P337+P313 If eye irritation persists: Get medical advice/attention. P390 Absorb spillage to prevent material damage.
2. Reagent 2: Warning. H290 May be corrosive to metals. P234 Keep only in original container. P280 Wear protective gloves/protective clothing/eye protection. P390 Absorb spillage to prevent material damage.
3. High homogentisic acid concentrations in urine samples lead to false results.
4. In very rare cases, samples of patients with gammopathy might give falsified results [11].
5. Please refer to the safety data sheets 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.
6. For professional use only!

Materials required but not provided

NaCl solution 9 g/L
General laboratory equipment

Specimen

Serum, heparin plasma, urine
Stability [5]

in serum /plasma:	7 days	at	4 – 25°C
	at least 3 months	at	–20°C
in urine:	2 days	at	20 – 25°C
	6 days	at	4 – 8°C
	6 months	at	–20°C

Dilute urine 1 + 49 with dist. water; multiply the result by 50. TruLab Urine controls must be prediluted the same way as patient samples.

Discard contaminated specimens! Only freeze once!

Assay Procedure

Application sheets for automated systems are available on request.

Wavelength	Hg 492 nm, (490 – 510 nm)
Optical path	1 cm
Temperature	20 – 25 °C/37°C
Measurement	Against reagent blank

Substrate start

	Blank	Sample or standard
Sample or standard	-	50 µL
Dist. Water	50 µL	-
Reagent 1	1000 µL	1000 µL
Mix, incubate 0 – 5 min., then add:		
Reagent 2	250 µL	250 µL
Mix and read absorbance A1 after 60 sec, read absorbance A2 after further 120 sec.		

ΔA = (A2 – A1) sample or standard

Sample start

	Blank	Sample or standard
Sample or standard	-	50 µL
Dist. Water	50 µL	-
Mono reagent	1000 µL	1000 µL
Mix and read absorbance A1 after 60 sec, read absorbance A2 after further 120 sec.		

ΔA = (A2 – A1) sample or standard

Calculation

With standard or calibrator

Serum/Plasma

$$\text{Creatinine [mg/dL]} = \frac{\Delta A \text{ Sample}}{\Delta A \text{ Std / Cal}} \times \text{Conc. Std / Cal [mg/dL]}$$

Urine

$$\text{Creatinine [mg/dL]} = \frac{\Delta A \text{ Sample}}{\Delta A \text{ Std / Cal}} \times \text{Conc. Std / Cal [mg/dL]} \times 50$$

Creatinine Clearance [mL/min/1.73 m^2] [7]

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

The calculated creatinine clearance refers to the average body surface of an adult (1.73 m^2).

Conversion factor

Creatinine [mg/dL] x 88.4 = Creatinine [µmol/L]

* fluid stable

Calibrators and Controls

For the calibration of automated photometric systems, DiaSys TruCal U calibrator is recommended. Calibrator values have been made traceable to 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). For internal quality control DiaSys TruLab N, P and TruLab Urine controls should be assayed.
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

Compensated method [3,4]

Picric acid which forms the colored complex reacts unspecifically with interfering serum components, so-called pseudo-creatinines. This leads to falsely elevated creatinine values in serum and plasma samples especially in the low measuring range. To compensate these interferences the calibrator value for the compensated method indicated in the value sheet of TruCal U has to be used for calculation. Additionally 0.3 mg/dL (27 µmol/L) has to be subtracted from the calculated creatinine value.
For use of the compensated method calibration with the calibrator TruCal U is strictly recommended. The method is applicable only for serum and plasma samples. The compensated method is traceable to GC-IDMS.

Performance Characteristics

Measuring range

The test has been developed to determine creatinine concentrations within a measuring range from 0.2 – 15 mg/dL (18 – 1330 µmol/L). When values exceed this range samples should be diluted 1 + 1 with NaCl solution (9 g/L) and the result multiplied by 2.

Sensitivity/Limit of Detection

The lower limit of detection is 0.2 mg/dL (17.7 µmol/L).

Specificity/Interferences

No interference was observed by ascorbic acid up to 30 mg/dL, hemoglobin up to 500 mg/dL and lipemia up to 2000 mg/dL triglycerides. Bilirubin interferes starting with a bilirubin concentration of 4 mg/dL. For further information on interfering substances refer to Young DS [10].

Precision (at 37°C)

Intra-assay precision n = 20	Mean [mg/dL]	SD [mg/dL]	CV [%]
Sample 1	0.56	0.01	1.30
Sample 2	1.24	0.01	0.83
Sample 3	6.73	0.06	0.93

Inter-assay precision n = 20	Mean [mg/dL]	SD [mg/dL]	CV [%]
Sample 1	0.81	0.03	3.63
Sample 2	1.60	0.01	0.87
Sample 3	5.73	0.05	0.85

Method Comparison

A comparison of DiaSys Creatinine FS (y) with a commercially available Jaffé method (x) using 68 human sera samples within a range of 0.6 – 10 mg/dL (53.0 – 884 µmol/L) gave following results:
y = 1.014 x – 0.031 mg/dL; r = 1.000

A comparison of DiaSys Creatinine FS compensated (y) with the enzymatic method DiaSys Creatinine PAP FS (x) using 65 human sera samples within a range of 0.5 – 4.3 mg/dL (44.2 – 380 µmol/L) gave following results:

y = 0.986 x + 0.043 mg/dL; r = 0.998

Reference Range

Serum/plasma, Jaffé-method not compensated

	mg/dL	µmol/L
Adults [1]		
Women	0.6 – 1.1	53 – 97
Men	0.7 – 1.3	62 – 115
Children [2,8]		
Neonate	0.5 – 1.2	44 – 106
Infant	0.4 – 0.7	35 – 62
Child	0.5 – 1.2	44 – 106

Serum/plasma, Jaffé-method compensated

	mg/dL	µmol/L
Adults [3]		
Women	0.5 – 0.9	44 – 80
Men	0.7 – 1.2	62 – 106
Children [9]		
Neonate	0.24 – 1.04	21 – 92
Infant	0.17 – 0.42	15 – 37
Child	0.24 – 0.87	21 – 77

24h urine [1]

Women	11 – 20 mg/kg/24h	97 – 177 µmol/kg/24h
Men	14 – 26 mg/kg/24h	124 – 230 µmol/kg/24h

Albumin/creatinine ratio (early morning urine) [12]**:**

< 30 mg/g Creatinine

Creatinine clearance [2]

Women	95 – 160 mL/min/1.73 m^2
Men	98 – 156 mL/min/1.73 m^2

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

Literature

1. Newman DJ, Price CP. Renal function and nitrogen metabolites. In: Burtis CA, Ashwood ER, editors. Tietz Textbook of Clinical Chemistry. 3rd ed. Philadelphia: W.B Saunders Company; 1999. p. 1204-1270.
2. Thomas L. Clinical Laboratory Diagnostics. 1st ed. Frankfurt: TH-Books Verlagsgesellschaft; 1998. p. 366-74.
3. Mazzachi BC, Peake MJ, Ehrhardt V. Reference Range and Method Comparison Studies for Enzymatic and Jaffé Creatine Assays in Plasma and Serum and Early Morning Urine. Clin. Lab. 2000; 46: 53-55.
4. Swanson AF, Swartzentruber M, Nolen PA et al. Multicenter Evaluation of the Boehringer Mannheim Compensated, Rate-Blanked Creatinine/Jaffe Application on BM/Hitachi Systems. Advances in Clinical Diagnostics. 1993. Boehringer Mannheim Corporation.
5. Guder WG, Zawta B. Recommendations of the Working group on Preanalytical Quality of the German Society for Clinical Chemistry and the German Society for Laboratory Medicine: The Quality of Diagnostic Samples. 1st ed Darmstadt: GIT Verlag 2001; p. 24-5,50-1.
6. Levey AS, Coresh J, Greene T, Marsh J et al: Expressing the Modification of Diet in Renal Disease Study Equation for Estimating Glomerular Filtration Rate with Standardized Serum Creatinine Values. Clin Chem 2007; 53 (4): 766-72.
7. Junge W, Wilke B, Halabi A, Klein G. 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.
8. Soldin SJ, Brugnara C, Wong EC, eds. Pediatric Reference Intervals. 6th ed. AACC Press, 2007: p. 77-78.
9. Schlebusch H, Liappis N, Klein G. Ultrasensitive CRP and Creatinine: Reference intervals from infancy to childhood. Clin Chem Lab Med. 2001; 39 Special supplement pp S1-S448; May 2001. PO-T042.
10. Young DS. Effects of Drugs on Clinical Laboratory Tests. 5th ed. Vol. 1 and 2. Washington, CD: The American Association for Clinical Chemistry Press 2000.
11. Bakker AJ, Mücke M. Gammopathy interference in clinical chemistry assays: mechanisms, detection and prevention. ClinChemLabMed 2007;45(9):1240-1243.
12. Dati F, Metzmann E. Proteins-Laboratory testing and clinical use. 1st ed. Holzheim: DiaSys Diagnostic Systems; 2005: p. 93.

Manufacturer

IVD CE

DiaSys Diagnostic Systems GmbH
Alte Strasse 9 65558 Holzheim Germany