CREP2

cobas®

Creatinine plus ver.2

Order information

REF	CONTENT		Analyzer(s) on which **cobas c** pack(s) can be used
03263991 190	Creatinine plus ver.2 250 tests	System-ID 07 6612 7	Roche/Hitachi **cobas c** 311, **cobas c** 501/502
10759350 190	Calibrator f.a.s. (12 x 3 mL)	Code 401	
10759350 360	Calibrator f.a.s. (12 x 3 mL, for USA)	Code 401	
12149435 122	Precinorm U plus (10 x 3 mL)	Code 300	
12149435 160	Precinorm U plus (10 x 3 mL, for USA)	Code 300	
12149443 122	Precipath U plus (10 x 3 mL)	Code 301	
12149443 160	Precipath U plus (10 x 3 mL, for USA)	Code 301	
10171743 122	Precinorm U (20 x 5 mL)	Code 300	
10171735 122	Precinorm U (4 x 5 mL)	Code 300	
10171778 122	Precipath U (20 x 5 mL)	Code 301	
10171760 122	Precipath U (4 x 5 mL)	Code 301	
03121313 122	Precinorm PUC (4 x 3 mL)	Code 240	
03121291 122	Precipath PUC (4 x 3 mL)	Code 241	
05117003 190	PreciControl ClinChem Multi 1 (20 x 5 mL)	Code 391	
05947626 190	PreciControl ClinChem Multi 1 (4 x 5 mL)	Code 391	
05947626 160	PreciControl ClinChem Multi 1 (4 x 5 mL, for USA)	Code 391	
05117216 190	PreciControl ClinChem Multi 2 (20 x 5 mL)	Code 392	
05947774 190	PreciControl ClinChem Multi 2 (4 x 5 mL)	Code 392	
05947774 160	PreciControl ClinChem Multi 2 (4 x 5 mL, for USA)	Code 392	
04489357 190	Diluent NaCl 9 % (50 mL)	System-ID 07 6869 3	

English

System information

cobas c 311/501 analyzers

CREA2: ACN 452 (serum, plasma, urine)

cobas c 502 analyzer

CREA2: ACN 8452 (serum, plasma)

CRE2U: ACN 8152 (urine)

Intended use

In vitro test for the quantitative determination of creatinine concentration in human serum, plasma and urine on Roche/Hitachi **cobas c** systems.

Summary[1,2,3,4,5]

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^2 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 Cockroft 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.[6,7,8,9]
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, 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.

Test principle

This enzymatic method is based on the conversion of creatinine with the aid of creatininase, creatinase, and sarcosine oxidase to glycine, formaldehyde and hydrogen peroxide. Catalyzed by peroxidase the liberated hydrogen peroxide reacts with 4-aminophenazone and HTIB[a] to form a quinone imine chromogen. The color intensity of the quinone imine chromogen formed is directly proportional to the creatinine concentration in the reaction mixture.

$$\text{creatinine} + H_2O \xrightarrow{\text{creatininase}} \text{creatine}$$

$$\text{creatine} + H_2O \xrightarrow{\text{creatinase}} \text{sarcosine} + \text{urea}$$

$$\text{sarcosine} + O_2 + H_2O \xrightarrow{\text{SOD}} \text{glycine} + \text{HCHO} + H_2O_2$$

$$H_2O_2 + \text{4-aminophenazone} + \text{HTIB} \xrightarrow{\text{POD}} \text{quinone imine chromogen} + H_2O + \text{HI}$$

Creatine of the sample is destroyed by creatinase, SOD and catalase during incubation in R1.

a) 2,4,6-triiodo-3-hydroxybenzoic acid

Reagents - working solutions

R1 TAPS buffer (N-Tris(hydroxymethyl)methyl-3-aminopropanesulfonic acid): 30 mmol/L, pH 8.1; creatinase (microorganisms): ≥ 332 µkat/L; sarcosine oxidase (microorganisms): ≥ 132 µkat/L; ascorbate oxidase (microorganisms): ≥ 33 µkat/L; catalase (microorganisms): ≥ 1.67 µkat/L; HTIB: 1.2 g/L; detergents; preservative

R3 TAPS buffer: 50 mmol/L, pH 8.0; creatininase (microorganisms): ≥ 498 µkat/L; peroxidase (horseradish): ≥ 16.6 µkat/L; 4-aminophenazone: 0.5 g/L; potassium hexacyanoferrate (II): 60 mg/L; detergent; preservative

R1 is in position B and R3 is in position C.

Precautions and warnings
For in vitro diagnostic use.
Exercise the normal precautions required for handling all laboratory reagents.
Disposal of all waste material should be in accordance with local guidelines.
Safety data sheet available for professional user on request.

For USA: For prescription use only.

Reagent handling
Ready for use

Storage and stability

CREP2

Shelf life at 2-8 °C:	See expiration date on **cobas c** pack label.
On-board in use and refrigerated on the analyzer:	8 weeks

Diluent NaCl 9 %

Shelf 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 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.

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	2-Point End		
Reaction time / Assay points	10 / 25-57		
Wavelength (sub/main)	700/546 nm		
Reaction direction	Increase		
Units	µmol/L (mg/dL, mmol/L)		
Reagent pipetting		Diluent (H_2O)	
R1	77 µL	–	
R3	38 µL	–	
Sample volumes	*Sample*	*Sample dilution*	
		Sample	*Diluent (NaCl)*
Normal	2 µL	–	–
Decreased	5 µL	15 µL	135 µL
Increased	2 µL	–	–

cobas c 501 **test definition**

Assay type	2-Point End		
Reaction time / Assay points	10 / 37-70		
Wavelength (sub/main)	700/546 nm		
Reaction direction	Increase		
Units	µmol/L (mg/dL, mmol/L)		
Reagent pipetting		Diluent (H_2O)	
R1	77 µL	–	
R3	38 µL	–	
Sample volumes	*Sample*	*Sample dilution*	
		Sample	*Diluent (NaCl)*
Normal	2 µL	–	–
Decreased	5 µL	15 µL	135 µL
Increased	2 µL	–	–

cobas c 502 **test definition**

Assay type	2-Point End		
Reaction time / Assay points	10 / 37-70		
Wavelength (sub/main)	700/546 nm		
Reaction direction	Increase		
Units	µmol/L (mg/dL, mmol/L)		
Reagent pipetting		Diluent (H_2O)	
R1	77 µL	–	
R3	38 µL	–	
Sample volumes	*Sample*	*Sample dilution*	
		Sample	*Diluent (NaCl)*
Normal	2 µL	–	–
Decreased	5 µL	15 µL	135 µL

Increased	4 µL	–	–

Application for urine

cobas c 311 **test definition**

Assay type	2-Point End		
Reaction time / Assay points	10/25-57		
Wavelength (sub/main)	700/546 nm		
Reaction direction	Increase		
Units	µmol/L (mg/dL, mmol/L)		
Reagent pipetting		Diluent (H_2O)	
R1	77 µL	–	
R3	38 µL	–	
Sample volumes	*Sample*	*Sample dilution*	
		Sample	*Diluent (NaCl)*
Normal	5 µL	3 µL	147 µL
Decreased	2 µL	3 µL	147 µL
Increased	5 µL	3 µL	147 µL

cobas c 501 **test definition**

Assay type	2-Point End		
Reaction time / Assay points	10 / 37-70		
Wavelength (sub/main)	700/546 nm		
Reaction direction	Increase		
Units	µmol/L (mg/dL, mmol/L)		
Reagent pipetting		Diluent (H_2O)	
R1	77 µL	–	
R3	38 µL	–	
Sample volumes	*Sample*	*Sample dilution*	
		Sample	*Diluent (NaCl)*
Normal	5 µL	3 µL	147 µL
Decreased	2 µL	3 µL	147 µL
Increased	5 µL	3 µL	147 µL

cobas c 502 **test definition**

Assay type	2-Point End		
Reaction time / Assay points	10 / 37-70		
Wavelength (sub/main)	700/546 nm		
Reaction direction	Increase		
Units	µmol/L (mg/dL, mmol/L)		
Reagent pipetting		Diluent (H_2O)	
R1	77 µL	–	
R3	38 µL	–	
Sample volumes	*Sample*	*Sample dilution*	
		Sample	*Diluent (NaCl)*
Normal	5 µL	3 µL	147 µL
Decreased	2 µL	3 µL	147 µL
Increased	10 µL	3 µL	147 µL

Calibration

Calibrators	S1: H_2O S2: C.f.a.s.
Calibration mode	Linear
Calibration frequency	Blank calibration • after 4 weeks during shelf life 2-point calibration • after reagent lot change • as required following quality control procedures

Traceability: This method has been standardized against ID/MS.

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.

Calculation

Roche/Hitachi **cobas c** 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

Limitations - interference

Criterion: Recovery within ± 10 % of initial values at creatinine concentrations of 80 µmol/L (0.9 mg/dL) in serum and 2500 µmol/L (28.3 mg/dL) in urine.

Serum/plasma

Icterus:[12] No significant interference up to an I index of 15 for conjugated bilirubin and 20 for unconjugated bilirubin (approximate conjugated bilirubin concentration: 257 µmol/L or 15 mg/dL; approximate unconjugated bilirubin concentration: 342 µmol/L or 20 mg/dL).

Hemolysis:[12] No significant interference up to an H index of 800 (approximate hemoglobin concentration: 497 µmol/L or 800 mg/dL).

Lipemia (Intralipid):[12] No significant interference up to an L index of 2000. There is a poor correlation between the L index (corresponds to turbidity) and triglycerides concentration.

Ascorbic acid: < 1.70 mmol/L or < 300 mg/L does not interfere.

Drugs: No interference was found at therapeutic concentrations using common drug panels.[13,14]

Exceptions: Rifampicin, Levodopa and Calcium dobesilate (e.g. Dexium) cause artificially low creatinine results. Dicynone (Etamsylate) at therapeutic concentrations may lead to falsely low results.[15]

N-ethylglycine at therapeutic concentrations and DL-proline at concentrations ≥ 1 mmol/L (≥ 115 mg/L) give falsely high results.

No significant interference up to a creatine level of 4 mmol/L (524 mg/L).

Hemolyzed samples from neonates, infants or adults with HbF values ≥ 600 mg/dL interfere with the test.[16]

2-Phenyl-1,3-indandion (Phenindion) at therapeutic concentrations interferes with the assay.

In very rare cases, gammopathy, in particular type IgM (Waldenström's macroglobulinemia), may cause unreliable results.[17]

Estimation of the glomerular filtration rate (GFR) on the basis of the Schwartz formula can lead to an overestimation.[18]

Acetaminophen intoxications are frequently treated with N-Acetylcysteine. N-Acetylcysteine at a plasma concentration above 333 mg/L and the Acetaminophen metabolite N-acetyl-p-benzoquinone imine (NAPQI) independently may cause falsely low results.

Venipuncture should be performed prior to the administration of Metamizole. Venipuncture immediately after or during the administration of Metamizole may lead to falsely low results. A significant interference may occur at any plasma Metamizole concentration.

Urine

Icterus: No significant interference up to a conjugated bilirubin concentration of 1197 µmol/L or 70 mg/dL.

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

Ascorbic acid < 22.7 mmol/L (< 4000 mg/L), 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 concentrations using common drug panels.[14]

Exceptions: Calcium dobesilate (e.g. Dexium), Levodopa and α-methyldopa cause artificially low creatinine results. Dicynone (Etamsylate) at therapeutic concentrations may lead to falsely low results.

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

Acetaminophen, Acetylcysteine and Metamizole are metabolized quickly. Therefore, interference from these substances is unlikely but cannot be excluded.

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 Roche/Hitachi **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 not required.

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

5-2700 µmol/L (0.06-30.5 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.

Urine

100-54000 µmol/L (1.1-610 mg/dL)

Determine samples having higher concentrations via the rerun function. Dilution of samples via the rerun function is a 1:2.5 dilution. Results from samples diluted using the rerun function are automatically multiplied by a factor of 2.5.

Lower limits of measurement

Lower detection limit of the test

Serum/plasma

5 µmol/L (0.06 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

100 µmol/L (1.1 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).

Expected values

Serum/plasma

Adults[19]		
Females	45-84 µmol/L	(0.51-0.95 mg/dL)
Males	59-104 µmol/L	(0.67-1.17 mg/dL)
Children[20]		
Neonates (premature)	29-87 µmol/L	(0.33-0.98 mg/dL)
Neonates (full term)	27-77 µmol/L	(0.31-0.88 mg/dL)
2-12 m	14-34 µmol/L	(0.16-0.39 mg/dL)
1-< 3 y	15-31 µmol/L	(0.18-0.35 mg/dL)
3-< 5 y	23-37 µmol/L	(0.26-0.42 mg/dL)
5-< 7 y	25-42 µmol/L	(0.29-0.47 mg/dL)
7-< 9 y	30-47 µmol/L	(0.34-0.53 mg/dL)
9-< 11 y	29-56 µmol/L	(0.33-0.64 mg/dL)
11-< 13 y	39-60 µmol/L	(0.44-0.68 mg/dL)
13-< 15 y	40-68 µmol/L	(0.46-0.77 mg/dL)

Urine

1st morning urine[19]		
Females	2.55-20.0 mmol/L	(29-226 mg/dL)
Males	3.54-24.6 mmol/L	(40-278 mg/dL)
24-hour urine[21]		
Females	6-13 mmol/24 h	(720-1510 mg/24 h)
Males	9-19 mmol/24 h	(980-2200 mg/24 h)
Creatinine clearance[21]	66-143 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.

Roche has not evaluated reference ranges in a pediatric population.

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:

Serum/plasma

Repeatability	*Mean*	*SD*	*CV*
	µmol/L (mg/dL)	*µmol/L (mg/dL)*	*%*
Precinorm U	96.1 (1.08)	0.9 (0.01)	0.9
Precipath U	341 (3.85)	2 (0.02)	0.6
Human serum 1	191 (2.16)	2 (0.02)	1.1
Human serum 2	398 (4.50)	4 (0.05)	1.0

Intermediate precision	*Mean*	*SD*	*CV*
	µmol/L (mg/dL)	*µmol/L (mg/dL)*	*%*
Precinorm U	94.9 (1.07)	1.4 (0.02)	1.4
Precipath U	338 (3.82)	4 (0.05)	1.1

Human serum 3	190 (2.15)	2 (0.02)	1.1
Human serum 4	395 (4.46)	5 (0.06)	1.2

Urine

Repeatability	*Mean*	*SD*	*CV*
	µmol/L (mg/dL)	*µmol/L (mg/dL)*	*%*
Control Level 1	7280 (82.3)	92 (1.0)	1.3
Control Level 2	14031 (159)	179 (2)	1.3
Human urine 1	17289 (195)	237 (3)	1.4
Human urine 2	7035 (79.5)	68 (0.8)	1.0

Intermediate precision	*Mean*	*SD*	*CV*
	µmol/L (mg/dL)	*µmol/L (mg/dL)*	*%*
Control Level 1	7219 (81.6)	112 (1.3)	1.5
Control Level 2	14018 (158)	212 (2)	1.5
Human urine 3	17326 (196)	244 (3)	1.4
Human urine 4	7008 (79.2)	104 (1.2)	1.5

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 using the corresponding reagent on a Roche/Hitachi 917 analyzer (x).

Serum/plasma

Sample size (n) = 63

Passing/Bablok[22]	Linear regression
y = 1.002x - 0.434 µmol/L	y = 0.991x + 2.94 µmol/L
τ = 0.978	r = 1.000

The sample concentrations were between 49 and 1891 µmol/L (0.55 and 21.4 mg/dL).

Urine

Sample size (n) = 75

Passing/Bablok[22]	Linear regression
y = 0.985x + 21.3 µmol/L	y = 0.977x + 80.0 µmol/L
τ = 0.990	r = 1.000

The sample concentrations were between 438 and 52577 µmol/L (4.95 and 594 mg/dL).

References

1 Thomas C, Thomas L. Labordiagnostik von Erkrankungen der Nieren und ableitenden Harnwege. In: Thomas L, ed. Labor und Diagnose, 6th ed. Frankfurt/Main: TH-Books 2005;520-585.

2 Lamb E, Newman DJ, Price CP. Kidney function tests In: Burtis CA, Ashwood ER, Bruns DE. Tietz textbook of clinical chemistry and molecular diagnostics. 4th ed. St.Louis, MO: Elsevier Saunders 2006;797-835.

3 http://www.kidney.org/

4 http://www.nkdep.nih.gov/

5 Lamb EJ, Tomson CRV, Roderick PJ. Estimating kidney function in adults using formulae. Ann Clin Biochem 2005;42:321-345.

6 Miller WG. Editorial on Estimating glomerular filtration rate. Clin Chem Lab Med 2009;47(9):1017-1019.

7 Schwartz GJ, Muñoz A, Schneider MF, et al. New Equations to Estimate GFR in Children with CKD. J Am Soc Nephrol 2009;20:629-637.

8 Schwartz GJ, Work DF. Measurement and Estimation of GFR in Children and Adolescents. Clin J Am Soc Nephrol 2009;4:1832–1843.

9 Staples A, LeBlond R, Watkins S, et al. Validation of the revised Schwartz estimating equation in a predominantly non-CKD population. Pediatr Nephrol 2010 Jul 22;25:2321-2326.

10 Guder W, Fonseca-Wollheim W, Ehret W, et al. Die Qualität Diagnostischer Proben, 6. Aufl. Heidelberg: BD Diagnostics, 2009.

11 Data on file at Roche Diagnostics.

12 Glick MR, Ryder KW, Jackson SA. Graphical Comparisons of Interferences in Clinical Chemistry Instrumentation. Clin Chem 1986;32:470-475.

13 Breuer J. Report on the Symposium “Drug effects in Clinical Chemistry Methods”. Eur J Clin Chem Clin Biochem 1996;34:385-386.

14 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;38:376-385.

15 Dastych M, Wiewiorka O, Benovska M. Ethamsylate (Dicynone) Interference in Determination of Serum Creatinine, Uric Acid, Triglycerides, and Cholesterol in Assays Involving the Trinder Reaction; In Vivo and In Vitro. Clin Lab 2014;60:1373-1376.

16 Mazzachi BC, Phillips JW, Peake MJ. Is the Jaffe creatinine assay suitable for neonates? Clin Biochem Revs 1998;19:82.

17 Bakker AJ, Mücke M. Gammopathy interference in clinical chemistry assays: mechanisms, detection and prevention. Clin Chem Lab Med 2007;45(9):1240-1243.

18 Filler G, Priem F, Lepage N, et al. β-Trace Protein, Cystatin C, β2-Microglobulin, and Creatinine Compared for Detecting Impaired Glomerular Filtration Rates in Children. Clin Chem 2002;48:729-736.

19 Mazzachi BC, Peake MJ, Ehrhardt V. Reference Range and Method Comparison Studies for Enzymatic and Jaffé Creatinine Assays in Plasma and Serum and Early Morning Urine. Clin Lab 2000;53-55.

20 Schlebusch H, Liappis N, Kalina E, et al. High Sensitive CRP and Creatinine: Reference Intervals from Infancy to Childhood. J Lab Med 2002;26:341-346.

21 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.

22 Bablok W, Passing H, Bender R, et al. A general regression procedure for method transformation. Application of linear regression procedures for method comparison studies in clinical chemistry, Part III. J Clin Chem Clin Biochem 1988 Nov;26(11):783-790.

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	Contents of kit
→	Volume after reconstitution or mixing
GTIN	Global Trade Item Number

FOR US CUSTOMERS ONLY: LIMITED WARRANTY

Roche Diagnostics warrants that this product will meet the specifications stated in the labeling when used in accordance with such labeling and will be free from defects in material and workmanship until the expiration date printed on the label. THIS LIMITED WARRANTY IS IN LIEU OF ANY OTHER WARRANTY, EXPRESS OR IMPLIED, INCLUDING ANY IMPLIED WARRANTY OF MERCHANTABILITY OR FITNESS FOR PARTICULAR PURPOSE. IN NO EVENT SHALL ROCHE DIAGNOSTICS BE LIABLE FOR INCIDENTAL, INDIRECT, SPECIAL OR CONSEQUENTIAL DAMAGES.

CREP2

Creatinine plus ver.2

CE

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