Roche

Diagnostics

EG-Konformitätserklärung/*EC Declaration of Conformity*

gemäß Anhang III der Richtlinie 98/79/EG des Europäischen Parlaments und des Rates vom 27. Oktober 1998
as per Annex III of Directive 98/79/EC of the European Parliaments and Council of 27 October 1998

Hersteller/*Manufacturer*:	Roche Diagnostics GmbH
Adresse/*Address:*	Roche Centralized Diagnostics Sandhofer Straße 116 D-68305 Mannheim

Die Roche Diagnostics GmbH erklärt, dass das Produkt/die Produktfamilie (bei rezepturgleichen Produkten)
Roche Diagnostics GmbH declares that the product/the product line (in case of products manufactured by identical recipes)

Produktname/*Product name*:	**ALP2S** Alkaline phosphatase acc. to IFCC Gen. 2
Art.-Nr./*Id. No.*:	04657373
Beschreibung/*Description*:	In vitro Test zur quantitativen Bestimmung der alkalischen Phosphatase in Humanserum und -plasma mit dem cobas c 111 System. *In vitro test for the quantitative determination of alkaline phosphatase in human serum and plasma on the cobas c 111 system.*

auf das/die sich diese Erklärung bezieht, den Forderungen der EG-Richtlinie 98/79/EG des Rates vom 27. Oktober 1998 (bzw. seine Umsetzung in nationales Recht der Mitgliedsstaaten in welchen das Produkt vermarktet werden soll) über In-vitro-Diagnostica entspricht.
to which this declaration relates fulfils the requirements of EC Directive 98/79/EC of the Council of 27 October 1998 (and its relevant transposition into the national laws of the Member States in which the device is intended to be placed on the market) concerning in-vitro diagnostic devices.

Mannheim, 02.11.2006

Roche Diagnostics GmbH

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EG-Konformitätserklärung/*EC Declaration of Conformity*

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Roche Diagnostics GmbH declares that the product/the product line (in case of products manufactured by identical recipes)

Produktname/*Product name*:	**BILT3** Bilirubin Total Gen.3
Art.-Nr./*Id. No.*:	**05795648**
Beschreibung/*Description*:	In-vitro-Test zur quantitativen Bestimmung von Gesamtbilirubin in Serum und Plasma von Erwachsenen und Neugeborenen mit dem **cobas c** 111 System. *In vitro test for the quantitative determination of total bilirubin in serum and plasma of adults and neonates on the **cobas c** 111 system.*

auf das/die sich diese Erklärung bezieht, den Forderungen der EG-Richtlinie 98/79/EG des Rates vom 27. Oktober 1998 (bzw. seine Umsetzung in nationales Recht der Mitgliedsstaaten in welchen das Produkt vermarktet werden soll) über In-vitro-Diagnostica entspricht.
to which this declaration relates fulfils the requirements of EC Directive 98/79/EC of the Council of 27 October 1998 (and its relevant transposition into the national laws of the Member States in which the device is intended to be placed on the market) concerning in-vitro diagnostic devices.

Mannheim, 01.02.2013
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EG-Konformitätserklärung/*EC Declaration of Conformity*

gemäß Anhang III der Richtlinie 98/79/EG des Europäischen Parlaments und des Rates vom 27. Oktober 1998
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Hersteller/*Manufacturer:*	Roche Diagnostics GmbH
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Die Roche Diagnostics GmbH erklärt, dass das Produkt/die Produktfamilie
Roche Diagnostics GmbH declares that the product/the product line

Produktname/*Product name*:	**ALTL** Alanine aminotransferase acc. IFCC with or without pyridoxal phosphate activation
Art.-Nr./*Cat. No.*:	**04718569190**
Beschreibung/*Description*:	In-vitro-Test zur quantitativen Bestimmung der Alaninaminotransferase (ALT) mit oder ohne Pyridoxalphosphataktivierung in Humanserum und -plasma mit dem **cobas c** 111 System. *In vitro test for the quantitative determination of alanine aminotransferase (ALT), with or without pyridoxal phosphate activation, in human serum and plasma on the **cobas c** 111 system.*

auf das/die sich diese Erklärung bezieht, den Forderungen der Richtlinie 98/79/EG des Europäischen Parlaments und des Rates vom 27. Oktober 1998 über In-vitro-Diagnostica (bzw. seine Umsetzung in nationales Recht der Mitgliedsstaaten in welchen das Produkt vermarktet werden soll) entspricht.
to which this declaration relates fulfils the requirements of Directive 98/79/EC of the European Parliament and Council of 27 October 1998 on in-vitro diagnostic medical devices (and its relevant transposition into the national laws of the Member States in which the device is intended to be placed on the market).

Mannheim, 25 August 2017

Roche Diagnostics GmbH

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UREAL

cobas®

Urea/BUN

Order information

REF	CONTENT		Analyzer(s) on which kit(s) can be used
04657616 190	Urea/BUN (4 × 100 tests)		**cobas c** 111
10759350 190	Calibrator f.a.s. (12 × 3 mL)	Code 401	
12149435 122	Precinorm U plus (10 × 3 mL)	Code 300	
12149443 122	Precipath U plus (10 × 3 mL)	Code 301	
05117003 190	PreciControl ClinChem Multi 1 (20 × 5 mL)	Code 391	
05947626 190	PreciControl ClinChem Multi 1 (4 × 5 mL)	Code 391	
05117216 190	PreciControl ClinChem Multi 2 (20 × 5 mL)	Code 392	
05947774 190	PreciControl ClinChem Multi 2 (4 × 5 mL)	Code 392	
04774230 190	NaCl Diluent 9 % (4 × 12 mL)	Code 951	
11930630 001	Chimneys		

English

System information
UREL: ACN 418
URELU: ACN 417

Intended use

In vitro test for the quantitative determination of urea/urea nitrogen in human serum, plasma and urine on the **cobas c** 111 system.

Summary[1]

Urea is the major end product of protein nitrogen metabolism. It is synthesized by the urea cycle in the liver from ammonia which is produced by amino acid deamination. Urea is excreted mostly by the kidneys but minimal amounts are also excreted in sweat and degraded in the intestines by bacterial action.

Determination of blood urea nitrogen is the most widely used screening test for renal function. When used in conjunction with serum creatinine determinations it can aid in the differential diagnosis of the three types of azotemia: prerenal, renal and postrenal.

Elevations in blood urea nitrogen concentration are seen in inadequate renal perfusion, shock, diminished blood volume (prerenal causes), chronic nephritis, nephrosclerosis, tubular necrosis, glomerular nephritis (renal causes) and urinary tract obstruction (postrenal causes). Transient elevations may also be seen during periods of high protein intake. Unpredictable levels occur with liver diseases.

Test principle

Kinetic test with urease and glutamate dehydrogenase[2,3,4,5]
Urea is hydrolyzed by urease to form ammonium and carbonate.

$$\text{Urea} + 2\ H_2O \xrightarrow{\text{Urease}} 2\ NH_4^+ + CO_3^{2-}$$

In the second reaction 2-oxoglutarate reacts with ammonium in the presence of glutamate dehydrogenase (GLDH) and the coenzyme NADH to produce L-glutamate. In this reaction two moles of NADH are oxidized to NAD for each mole of urea hydrolyzed.

$$NH_4^+ + \text{2-oxoglutarate} + \text{NADH} \xrightarrow{\text{GLDH}} \text{L-glutamate} + NAD^+ + H_2O$$

The rate of decrease in the NADH concentration is directly proportional to the urea concentration in the specimen and is measured photometrically.

Reagents - working solutions

R1 TRIS buffer: 220 mmol/L, pH 8.6; 2-oxoglutarate: 73 mmol/L; NADH: 2.5 mmol/L; ADP: 6.5 mmol/L; urease (jack bean): ≥ 300 µkat/L; GLDH (bovine liver): ≥ 80 µkat/L; preservative

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.

Reagent handling

Ready for use

Under conditions of extreme humidity, condensation may lead to a dilution of the reagent that affects the measurements. Hence under environmental conditions in which temperature and humidity are equal to, or in excess of 25 °C/80 %, 28 °C/70 %, 30 °C/60 % or 32 °C/55 % a chimney (Cat. No. 11930630 001) should be used to reduce the condensation rate. Place a white chimney in R1. The chimneys can be reused for reagent bottles within the same kit. However, to avoid contamination of the reagent with detergent or dilution of the reagent with water it is not permitted to wash the chimneys before reuse.

Storage and stability

UREAL

Shelf life at 2-8 °C:	See expiration date on reagent
On-board in use and refrigerated on the analyzer:	4 weeks

NaCl Diluent 9 %

Shelf life at 2-8 °C:	See expiration date on reagent
On-board in use and refrigerated on the analyzer:	4 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, K_3-EDTA plasma. Do not use ammonium heparin.
Urine

Bacterial growth in the specimen and high atmospheric ammonia concentration as well as contamination by ammonium ions may cause erroneously elevated results.

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.

Centrifuge samples containing precipitates before performing the assay.

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

Stability in *serum/plasma*:[6]	7 days at 20-25 °C
	7 days at 2-8 °C
	1 year at (-15)-(-20) °C

Stability in *urine*:[6]	2 days at 20-25 °C
	7 days at 2-8 °C
	1 year at (-15)-(-20) °C

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, plasma and urine

cobas c 111 **test definition**

Measuring mode	Absorbance
Abs. calculation mode	Kinetic
Reaction direction	Decrease
Wavelength A/B	340/409 nm
Calc. first/last	10/13
Unit	mmol/L
Serum, plasma	
Reaction mode	R-S
Urine	
Reaction mode	R-S
Predilution factor	50

Pipetting parameters

		Diluent (H_2O)
R	50 µL	95 µL
Sample	2 µL	98 µL
Total volume	245 µL	

Calibration

Calibrator	Calibrator f.a.s. Deionized water is used automatically by the instrument as the zero calibrator.
Calibration mode	Linear regression
Calibration interval	Each lot 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.

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

Quantitative urine controls are recommended for routine quality control.

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

The **cobas c** 111 analyzer automatically calculates the analyte concentration of each sample.

Conversion factors:

mmol/L urea × 6.006 = mg/dL urea

mmol/L urea × 2.801 = mg/dL urea nitrogen

mmol/L urea = mmol/L urea nitrogen

mg/dL urea × 0.167 = mmol/L urea

mg/dL urea × 0.467 = mg/dL urea nitrogen

mg/dL urea × 0.167 = mmol/L urea nitrogen

Limitations - interference

Criterion: Recovery within ± 10 % of initial value at a urea concentration of 8.3 mmol/L (49.8 mg/dL urea, 23.2 mg/dL urea nitrogen) in serum/plasma and at a urea concentration of 150 mmol/L (901 mg/dL urea, 421 mg/dL urea nitrogen) in urine.

Serum, plasma

Icterus:[7] No significant interference up to an I index of 60 for conjugated and unconjugated bilirubin (approximate conjugated and unconjugated bilirubin concentration: 1026 µmol/L or 60 mg/dL).

Hemolysis:[7] No significant interference up to an H index of 1000 (approximate hemoglobin concentration: 621 µmol/L or 1000 mg/dL).

Lipemia (Intralipid):[7] No significant interference up to an L index of 2000. There is poor correlation between the L index (corresponds to turbidity) and triglycerides concentration.

Ammonium ions may cause erroneously elevated results.

Drugs: No interference was found at therapeutic concentrations using common drug panels.[8,9]

In very rare cases, gammopathy, in particular type IgM (Waldenström's macroglobulinemia), may cause unreliable results.[10]

Urine

Drugs: No interference was found at therapeutic concentrations using common drug panels.[9]

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 the **cobas c** 111 analyzer. For information about test combinations requiring special wash steps, please refer to the latest version of the carry-over evasion list found with the CLEAN Method Sheet and the operator's 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

0.5-40 mmol/L (3.0-240 mg/dL urea, 1.40-112 mg/dL urea nitrogen)

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

1.0-2000 mmol/L (6-12000 mg/dL urea, 2.8-5600 mg/dL urea nitrogen)

Determine samples having higher concentrations via the rerun function. Dilution of samples via the rerun function is a 1:3 dilution. Results from samples diluted using the rerun function are automatically multiplied by a factor of 3.

Lower limits of measurement

Serum, plasma

Lower detection limit of the test:
0.5 mmol/L (3.0 mg/dL urea, 1.40 mg/dL urea nitrogen)

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
Lower detection limit of the test:
1.0 mmol/L (6 mg/dL urea, 2.8 mg/dL urea nitrogen)

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

Urea

Serum, plasma[11]		
Adults	2.76-8.07 mmol/L	(16.6-48.5 mg/dL)
Urine[12]		
24-hour urine	428-714 mmol/24 h (25.7-42.9 g/24 h), corresponding to 286-595 mmol/L (1.71-3.57 g/dL)[a)]	

a) Based on average urine output of 1.2-1.5 L/24 h

Urea nitrogen (BUN)

Serum/plasma[12]		
Adult (18-60 years)	2.14-7.14 mmol/L	(6-20 mg/dL)
Adult (60-90 years)	2.86-8.21 mmol/L	(8-23 mg/dL)
Infant (< 1 year)	1.43-6.78 mmol/L	(4-19 mg/dL)
Infant/child	1.79-6.43 mmol/L	(5-18 mg/dL)
Urine[12]		
24-hour urine:	428-714 mmol/24 h (12-20 g/24 h), corresponding to 286-595 mmol/L (801-1666 mg/dL)[a)]	

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

Specific performance data

Representative performance data on the **cobas c** 111 analyzer are given below. Results obtained in individual laboratories may differ.

Precision

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, 10 days). The following results were obtained:

Serum, plasma

Repeatability	*Mean* mmol/L (mg/dL urea)	*SD* *mmol/L (mg/dL urea)*	*CV* *%*
Precinorm U	6.53 (39.2)	0.07 (0.4)	1.1
Precipath U	23.3 (140)	0.1 (1)	0.6
Human serum 1	3.75 (22.5)	0.05 (0.3)	1.2
Human serum 2	35.3 (212)	0.3 (2)	0.7

Intermediate precision	*Mean* mmol/L (mg/dL urea)	*SD* *mmol/L (mg/dL urea)*	*CV* *%*
Precinorm U	6.33 (38.0)	0.06 (0.4)	0.9
Precipath U	22.3 (134)	0.2 (1)	1.1
Human serum 3	4.84 (29.1)	0.05 (0.3)	1.0
Human serum 4	32.3 (194)	0.3 (2)	0.8

Urine

Repeatability	*Mean* mmol/L (mg/dL urea)	*SD* *mmol/L (mg/dL urea)*	*CV* *%*
Control level 1	164 (984)	2 (13)	1.3
Control level 2	262 (1574)	3 (16)	1.0
Control level 3	286 (1720)	3 (19)	1.1
Urine sample 1	121 (729)	2 (15)	2.0
Urine sample 2	30.6 (183)	0.9 (5)	3.0
Urine sample 3	535 (3211)	5 (30)	0.9
Urine sample 4	1636 (9826)	14 (85)	0.9

Method comparison

Urea values for human samples obtained on the **cobas c** 111 analyzer (y) were compared with those determined on a COBAS INTEGRA 400 analyzer (x), using the corresponding reagent.

Serum, plasma
Sample size (n) = 71

Passing/Bablok[13]	Linear regression
y = 1.014x - 0.006 mmol/L	y = 1.011x + 0.053 mmol/L
τ = 0.987	r = 0.999

The sample concentrations were between 1.35 and 38.6 mmol/L (8.1 and 232 mg/dL urea).

Urine
Sample size (n) = 86

Passing/Bablok[13]	Linear regression
y = 0.966x + 0.316 mmol/L	y = 0.954x + 4.56 mmol/L
τ = 0.976	r = 0.999

The sample concentrations were between 30.6 and 1909.3 mmol/L (183.8 and 1104 mg/dL urea) on the reference system (x).

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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.

Symbols

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

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

CE

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