UREAL

Urea/BUN

Materials provided

REF		CONTENT	Analyzer(s) on which cobas c pack(s) can be used
05171873190*	05171873500	Urea/BUN (1900 tests)	**cobas** c 701/702
05171873214*	05171873500	Urea/BUN (1900 tests)	**cobas** c 701/702

* Some kits shown may not be available in all countries.

For reagents, refer to the "Reagents" section.

Materials required (but not provided)

REF	Description	Code
10759350190	Calibrator f.a.s. (12 × 3 mL)	401
05117003190	PreciControl ClinChem Multi 1 (20 × 5 mL)	391
05947626190	PreciControl ClinChem Multi 1 (4 × 5 mL)	391
05117216190	PreciControl ClinChem Multi 2 (20 × 5 mL)	392
05947774190	PreciControl ClinChem Multi 2 (4 × 5 mL)	392
05172152190	Diluent NaCl 9 % (119 mL)	System-ID 08 6869 3
	General laboratory equipment	

System information

Short name	ACN (application code number)	Description
UREAL	8418	serum, plasma
U-BUN	8421	serum, plasma
URELU	8417	urine
UBUNU	8428	urine
SUREA	8419	STAT, reaction time: 5, serum, plasma
SUBUN	8427	STAT, reaction time: 5, serum, plasma
SUREU	8420	STAT, reaction time: 5, urine
SBUNU	8429	STAT, reaction time: 5, urine

Intended use

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

Summary

Measurements of urea/urea nitrogen in human serum, plasma and urine, performed with this assay, are used as screening tests and as an aid in diagnosis and monitoring of renal function.

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.[1]

Serum urea mass concentration is either specified for the complete urea molecule or for nitrogen equivalents [blood urea nitrogen (BUN)].[2] Determination of blood urea nitrogen is primarily used as a 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. The urea to creatinine ratio has been proposed as a crude discriminator between prerenal and intrinsic azotemia.[1]

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. Liver diseases may lead to unpredictable blood urea nitrogen concentrations, including abnormally low levels. Low blood urea nitrogen concentrations are not common, but can be found in cases such as malnutrition, lack of protein in the diet, or overhydration.[1,3]

Test principle

Kinetic test with urease and glutamate dehydrogenase.[4,5,6,7]

Urea is hydrolyzed by urease to form ammonium and carbonate.

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

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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.

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

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

Reagents

R1	NaCl 9 %
R3 (STAT R2)	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; nonreactive stabilizers

R1 is in position C and R3 (STAT R2) is in position B.

Warnings and precautions

For in vitro diagnostic use for laboratory professionals. Exercise the normal precautions required for handling all laboratory reagents.

Infectious or microbial waste

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

Environmental hazards

Apply all relevant local disposal regulations to determine safe disposal.

The Safety Data Sheet is available for professional users on request.

Storage and stability

Shelf life at 2-8 °C	See expiration date on **cobas** c pack label.
On-board in use and refrigerated on the analyzer	4 weeks
On-board on the Reagent Manager	24 hours

Calibration

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

The calibration interval may be extended based on acceptable calibration verification values determined by the laboratory.

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

Quality control

Serum/plasma

For quality control, use the control materials listed in the “Materials required (but not provided)” section or other suitable control material.

Urine

Quantitative urine controls are recommended for routine quality control.

Adjust the limits and control intervals based on the laboratory’s individual requirements. If values fall outside the limits, each laboratory is advised to establish corrective measures.

Follow the applicable government regulations and local guidelines.

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. Do not use ammonium heparin.

Specimens derived from capillary blood were found acceptable.[8]

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Urea/BUN

The sample types listed were tested with a selection of sample collection tubes that were commercially available at the time of testing. 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

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

Stability in *serum/plasma*:[9]	7 days at 15-25 °C
	7 days at 2-8 °C
	1 year at (-15)-(-25) °C

Freeze only once.

Stability in *urine*:[9]	2 days at 15-25 °C
	7 days at 2-8 °C
	1 month at (-15)-(-25) °C

Freeze only once.

Centrifuge samples containing precipitates before performing the assay.

Refer to the "Limitations and interferences" section for details on possible sample interferences.

Test procedure

The product is ready for use.

For optimum performance of the assay, follow the instructions given in this document for the corresponding analyzer. For analyzer-specific assay instructions, refer to the corresponding User Guide.

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 701/702 **test definition**			
Assay type	Rate A		
Reaction time / Assay points	10/23-29 (STAT 5/11-17)		
Wavelength (sub/main)	700/340 nm		
Reaction direction	Decrease		
Units	mmol/L (mg/dL, g/L)		
Reagent pipetting		Diluent (H_2O)	
R1	10 µL	90 µL	
R3 (STAT R2)	38 µL	108 µL	
Sample volumes	*Sample*	*Sample dilution*	
		Sample	*Diluent (NaCl)*
Normal	2 µL	–	–
Decreased	4 µL	20 µL	100 µL
Increased	4 µL	–	–

Application for urine

cobas c 701/702 **test definition**			
Assay type	Rate A		
Reaction time / Assay points	10/23-29 (STAT 5/11-17)		
Wavelength (sub/main)	700/340 nm		
Reaction direction	Decrease		
Units	mmol/L (mg/dL, g/L)		
Reagent pipetting		Diluent (H_2O)	
R1	10 µL	90 µL	
R3 (STAT R2)	38 µL	108 µL	

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Urea/BUN

Sample volumes	*Sample*	*Sample dilution*	
		Sample	*Diluent (NaCl)*
Normal	2 µL	3 µL	147 µL
Decreased	2 µL	2 µL	178 µL
Increased	2 µL	–	–

Calculation

The **cobas** c systems automatically calculate the analyte concentration of each sample.

Conversion factors:
mmol/L urea × 6.006 = mg/dL urea
mmol/L urea × 0.06006 = g/L urea
mmol/L urea nitrogen × 2.801 = mg/dL urea nitrogen
mmol/L urea nitrogen × 0.02801 = g/L urea nitrogen
mg/dL urea × 0.467 = mg/dL urea nitrogen

When 24-hour urine is used as the specimen, multiply the result by the 24-hour volume to obtain values in g or mmol/24 hours.

Limitations and interferences

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

Serum/plasma

Criterion: recovery within ± 0.83 mmol/L of initial values for samples ≤ 8.3 mmol/L and within ± 10 % for samples > 8.3 mmol/L.

Icterus:[11] no significant interference up to an I index of 60 (approximate conjugated and unconjugated bilirubin concentration: 1026 µmol/L or 60 mg/dL).

Hemolysis:[11] no significant interference up to an H index of 1000 (approximate hemoglobin concentration: 621 µmol/L or 1000 mg/dL).

Lipemia (Intralipid):[11] no significant interference up to an L index of 1000. There is poor correlation between the L index (corresponds to turbidity) and the triglycerides concentration.

Ammonium ions may cause erroneously elevated results.

Drugs: No interference was found at therapeutic concentrations using common drug panels.[12,13]

Urine

Criterion: recovery within ± 15 mmol/L of initial values for samples ≤ 150 mmol/L and within ± 10 % for samples > 150 mmol/L.

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

For diagnostic purposes, always assess the results 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 **cobas** c systems. All special wash programming necessary for avoiding carryover is available via **cobas** link. In certain cases, manual input is required. The latest version of the carryover evasion list can be found on the NaOHD - SMS - SmpCln1+2 - SCCS Method Sheet. For further instructions, refer to the User Guide.

Where required, special wash / carryover 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, 1.4-112 mg/dL urea nitrogen)

Determine samples that have 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.

Urine

1-2000 mmol/L (6-12000 mg/dL urea, 2.8-5600 mg/dL urea nitrogen)

Determine samples that have higher concentrations via the rerun function. Dilution of samples via the rerun function is a 1:1.8 dilution. Results from samples diluted using the rerun function are automatically multiplied by a factor of 1.8.

Determine samples having concentrations lower than the technical limit of 40 mmol/L (240 mg/dL urea and 112 mg/dL urea nitrogen) via the rerun function. Samples are measured undiluted.

Lower limits of measurement

Lower detection limit of the test:

UREAL

Urea/BUN

Serum/plasma

0.5 mmol/L (3.0 mg/dL urea, 1.4 mg/dL urea nitrogen)

The lower detection limit represents the lowest measurable analyte level that can be distinguished from 0. The lower detection limit is calculated as the value lying 3 standard deviations above the value of the lowest standard (standard 1 + 3 SD, repeatability, n = 21).

Values below the lower detection limit (< 0.5 mmol/L) will not be flagged by the instrument.

Urine

1 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 0. The lower detection limit is calculated as the value lying 3 standard deviations above the value of the lowest standard (standard 1 + 3 SD, repeatability, n = 21).

Values below the lower detection limit (< 1 mmol/L) will not be flagged by the instrument.

Expected values

Urea

Serum/plasma[14]

Adults	2.76-8.07 mmol/L	(16.6-48.5 mg/dL)

Urine

24-hour urine[15]	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[15]

Adults (18-60 years)	2.14-7.14 mmol/L	6-20 mg/dL
Adults (60-90 years)	2.86-8.21 mmol/L	8-23 mg/dL
Infants (< 1 year)	1.43-6.78 mmol/L	4-19 mg/dL
Infants/children	1.79-6.43 mmol/L	5-18 mg/dL

Urine

24-hour urine[15]	428-714 mmol/24 h (12-20 g/24 h), corresponding to 286-595 mmol/L (801-1666 mg/dL)[A)]

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

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

Specific performance data

Representative performance data on the analyzers is given below. Results obtained in individual laboratories may differ from the representative performance data.

Precision

Precision was determined using human samples and controls based on 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 on the **cobas** c 701 analyzer:

Serum/plasma

UREAL/U-BUN:

Repeatability	Mean mmol/L (mg/dL urea)	SD mmol/L (mg/dL urea)	CV %
Precinorm U	7.10 (42.6)	0.07 (0.4)	0.9
Precipath U	26.3 (158)	0.3 (2)	1.1
Human serum A	7.20 (43.2)	0.09 (0.5)	1.2
Human serum B	16.4 (98.5)	0.1 (0.6)	0.7
Human serum C	35.1 (210)	0.3 (2)	0.7

SUREA/SUBUN:

UREAL

Urea/BUN

Repeatability	Mean mmol/L (mg/dL urea)	SD mmol/L (mg/dL urea)	CV %
Precinorm U	7.00 (42.0)	0.06 (0.4)	0.9
Precipath U	26.2 (157)	0.2 (1)	0.9
Human serum A	7.10 (42.6)	0.07 (0.4)	1.0
Human serum B	16.4 (98.5)	0.1 (0.6)	0.8
Human serum C	35.0 (210)	0.2 (1)	0.6

UREAL/U-BUN + SUREA/SUBUN:

Intermediate precision	Mean mmol/L (mg/dL urea)	SD mmol/L (mg/dL urea)	CV %
Precinorm U	6.66 (40.0)	0.08 (0.5)	1.2
Precipath U	23.2 (139)	0.3 (2)	1.1
Human serum 3	9.13 (54.8)	0.10 (0.6)	1.1
Human serum 4	14.9 (89.5)	0.2 (1.2)	1.3

Urine

URELU/UBUNU:

Repeatability	Mean mmol/L (mg/dL urea)	SD mmol/L (mg/dL urea)	CV %
Control level 1	154 (925)	2 (12)	1.4
Control level 2	250 (1501)	2 (12)	1.0
Human urine A	110 (661)	2 (12)	2.0
Human urine B	350 (2102)	3 (18)	0.8
Human urine C	1877 (11273)	15 (90)	0.8

SUREU/SBUNU:

Repeatability	Mean mmol/L (mg/dL urea)	SD mmol/L (mg/dL urea)	CV %
Control level 1	148 (889)	3 (18)	1.9
Control level 2	246 (1477)	3 (18)	1.2
Human urine A	107 (643)	2 (12)	1.5
Human urine B	345 (2072)	2 (12)	0.7
Human urine C	1875 (11261)	13 (78)	0.7

URELU/UBUNU + SUREU/SBUNU:

Intermediate precision	Mean mmol/L (mg/dL urea)	SD mmol/L (mg/dL urea)	CV %
Control level 1	154 (925)	4 (24)	2.7
Control level 2	280 (1682)	6 (36)	2.3
Human urine 3	316 (1898)	6 (36)	2.0
Human urine 4	133 (799)	3 (18)	2.4

Results for intermediate precision were obtained on the **cobas** c 501 analyzer.

The data obtained on the **cobas** c 501 analyzer are representative for the **cobas** c 701 analyzer.

Method comparison

Urea values for human serum, plasma and urine samples obtained on a **cobas** c 701 analyzer (y) were compared with values determined on **cobas** c 501 analyzer (x), using the corresponding reagent.

Serum/plasma

UREAL/U-BUN:

Sample size (n) = 114

Passing/Bablok[16]	Linear regression
y = 1.000x + 0.000 mmol/L	y = 1.004x – 0.077 mmol/L
τ = 0.989	r = 0.999

The sample concentrations were between 3.10 and 39.6 mmol/L (18.6 and 238 mg/dL urea).

SUREA/SUBUN:

Sample size (n) = 114

Passing/Bablok[16]	Linear regression
y = 1.000x + 0.10 mmol/L	y = 1.004x + 0.09 mmol/L
τ = 0.984	r = 0.999

The sample concentrations were between 2.9 and 39.5 mmol/L (17.4 and 237 mg/dL urea).

Urine

URELU/UBUNU:

Sample size (n) = 134

Passing/Bablok[16]	Linear regression
y = 0.983x – 2.55 mmol/L	y = 0.988x – 5.15 mmol/L
τ = 0.977	r = 1.000

The sample concentrations were between 11.7 and 1995 mmol/L (70.3 and 11982 mg/dL urea).

SUREU/SBUNU:

Sample size (n) = 135

Passing/Bablok[16]	Linear regression
y = 0.987x – 5.01 mmol/L	y = 1.021x – 19.99 mmol/L
τ = 0.973	r = 0.999

The sample concentrations were between 11.0 and 1965 mmol/L (66.1 and 11802 mg/dL urea).

Additional information

Additions, deletions, or changes are indicated by a change bar in the margin.

A point (period/stop) is always used in the English version of a Method Sheet as the decimal separator to mark the boundary between the integral and the fractional parts of a decimal numeral. The translated Method Sheets use decimal commas. Labels only use the decimal point as separator. Separators for thousands are not used.

Report any serious incident that has occurred in relation to the device to the manufacturer and the competent authority of the member state in which the user and/or patient is established.

Symbols

In addition to the ISO 15223-1 standard, Roche Diagnostics uses the following symbols and signs:

CONTENT	Contents of kit
→	Volume for reconstitution
GTIN	Global Trade Item Number
Rx only	For USA: Caution: Federal law restricts this device to sale by or on the order of a physician.

References

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CE 0123

Roche Diagnostics GmbH
Sandhofer Strasse 116
68305 Mannheim, Germany
www.roche.com
+800 5505 6606

Change log

For this document version only:

Due to technical reasons, changes that have been made since the last version of this document are listed in the following table instead of indicated by change bars in the margin.

Section headers are indicated in bold letters.

In addition to the changes listed in the table below, this method sheet version contains several editorial and layout updates.

Section	Current version	Previous version
Materials provided	**Materials provided**	**Order information** **Materials provided**
Materials provided	**Materials provided** without System-ID	**Order information** with System-ID
Materials required (but not provided)	**Materials required (but not provided)**	**Order information** **Materials required (but not provided)**
Materials required (but not provided)	outphased: REF 12149435122 Precinorm U plus REF 12149443122 Precipath U plus	with: REF 12149435122 Precinorm U plus REF 12149443122 Precipath U plus
Reagents	**Reagents**	**Reagents - working solutions**
Warnings and precautions	**Warnings and precautions**	**Precautions and warnings**
Specimen collection and preparation	Specimens derived from capillary blood were found acceptable. [Collier BB et al.]	
Test procedure	**Test procedure**	**Reagent handling** **Assay**
Limitations and interferences	**Limitations and interferences**	**Limitations - interference**

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Section	Current version	Previous version
Additional information	**Additional information**	
Additional information	A point (period/stop) is always used in the English version of a Method Sheet as the decimal separator to mark the boundary between the integral and the fractional parts of a decimal numeral. The translated Method Sheets use decimal commas. Labels only use the decimal point as separator. Separators for thousands are not used.	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.
References	Collier BB, Brandon WC, Chappell MR, et al. Maximizing Microsampling: Measurement of Comprehesnive Metabolic and Lipid Panels Using a Novel Capillary Blood Collection Device. JALM 2023 Nov;8(6):1115-1126.	