UREAL

cobas®

Urea/BUN

Order information

REF	CONTENT		Analyzer(s) on which **cobas c** pack(s) can be used
05171873 190	Urea/BUN (1900 tests)	System-ID 05 6303 9	**cobas c** 701/702
10759350 360	Calibrator f.a.s. (12 x 3 mL)	Code 401	
12149435 160	Precinorm U plus (10 x 3 mL)	Code 300	
12149443 160	Precipath U plus (10 x 3 mL)	Code 301	
05947626 160	PreciControl ClinChem Multi 1 (4 x 5 mL)	Code 391	
05947774 160	PreciControl ClinChem Multi 2 (4 x 5 mL)	Code 392	
05172152 190	Diluent NaCl 9 % (119 mL)	System-ID 08 6869 3	

English

For use in the USA only

System information

UREAL: ACN 8418 (serum, plasma)
U-BUN: ACN 8421 (serum, plasma)
URELU: ACN 8417 (urine)
UBUNU: ACN 8428 (urine)
SUREA: ACN 8419 (STAT, reaction time: 5, serum, plasma)
SUBUN: ACN 8427 (STAT, reaction time: 5, serum, plasma)
SUREU: ACN 8420 (STAT, reaction time: 5, urine)
SBUNU: ACN 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 Roche/Hitachi **cobas c** systems.

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	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.

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: Caution: Federal law restricts this device to sale by or on the order of a physician.

Reagent handling

Ready for use

Storage and stability

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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

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:	4 weeks
On-board on the Reagent Manager:	24 hours

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. Do not use ammonium heparin.

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

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*:[6]	7 days at 20-25 °C
	7 days at 4-8 °C
	1 year at -20 °C
Stability in *urine*:[6]	2 days at 20-25 °C
	7 days at 4-8 °C
	1 month at -20 °C

Centrifuge samples containing precipitates before performing the assay.

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

Sample stability claims were established by experimental data by the manufacturer or based on reference literature and only for the temperatures/time frames as stated in the method sheet. It is the responsibility of the individual laboratory to use all available references and/or its own studies to determine specific stability criteria for its laboratory.

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 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	
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	–	–

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

Calibration interval may be extended based on acceptable verification of calibration by the laboratory.

Traceability: This method has been standardized against SRM 912.

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

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

Conversion factors:	mmol/L urea x 6.006 = mg/dL urea
	mmol/L urea x 0.06006 = g/L urea
	mmol/L urea nitrogen x 2.801 = mg/dLurea nitrogen
	mmol/L urea nitrogen x 0.02801 = g/L urea nitrogen
	mg/dL urea x 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 - 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. Recovery within ± 10 % for drug interference.

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 1000. 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 **cobas c** systems. All special wash programming necessary for avoiding carry-over is available via the **cobas** link, manual input is required in certain cases. The latest version of the carry-over evasion list can be found with the NaOHD/SMS/SmpCln1+2/SCCS Method Sheet and for further instructions refer to the operator's manual.

Where required, special wash/carry-over evasion programming must be implemented prior to reporting results with this test.

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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 having higher concentrations via the rerun function. Dilution of samples via the rerun function is a 1:3 dilution. Results from samples diluted by 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 having higher concentrations via the rerun function. Dilution of samples via the rerun function is a 1:1.8 dilution. Results from samples diluted by 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

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 zero. It is calculated as the value lying 3 standard deviations above that 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 zero. It is calculated as the value lying 3 standard deviations above that 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:[11]

Serum, plasma

Adults (18-60 y)	2.1-7.1 mmol/L	(12.6-42.6 mg/dL)
Adults (60-90 y)	2.9-8.2 mmol/L	(17.4-49.2 mg/dL)

Urine

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 an average urine output of 1.2-1.5 L/24 h

Urea nitrogen (BUN):[11]

Serum, plasma

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

Roche has not evaluated reference ranges in a pediatric population.

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 analyzers 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 (*serum/plasma:* 3 aliquots per run, 1 run per day, 21 days; *urine:* 3 aliquots per run, 1 run per day, 10 days). The following results were obtained:

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:

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

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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 master system **cobas c** 501 analyzer.

Method comparison

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

Serum/plasma
UREAL/U-BUN:
Sample size (n) = 114

Passing/Bablok[12]	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[12]	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[12]	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[12]	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).

References

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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
→	Volume after reconstitution or mixing
GTIN	Global Trade Item Number

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