

Order information

REF	CONTENT	Analyzer(s) on which cobas c pack(s) can be used
04460715 190	Urea/BUN (500 tests)	System-ID 07 6303 9 COBAS INTEGRA 400 plus COBAS INTEGRA 800
10759350 190	Calibrator f.a.s. (12 × 3 mL)	System-ID 07 3718 6
10759350 360	Calibrator f.a.s. (12 × 3 mL, for USA)	System-ID 07 3718 6
12149435 122	Precinorm U plus (10 × 3 mL)	System-ID 07 7999 7
12149435 160	Precinorm U plus (10 × 3 mL, for USA)	System-ID 07 7999 7
12149443 122	Precipath U plus (10 × 3 mL)	System-ID 07 8000 6
12149443 122	Precipath U plus (10 × 3 mL, for USA)	System-ID 07 8000 6
10171743 122	Precinorm U (20 × 5 mL)	System-ID 07 7997 0
10171735 122	Precinorm U (4 × 5 mL)	System-ID 07 7997 0
10171778 122	Precipath U (20 × 5 mL)	System-ID 07 7998 9
10171760 122	Precipath U (4 × 5 mL)	System-ID 07 7998 9
05117003 190	PreciControl ClinChem Multi 1 (20 × 5 mL)	System-ID 07 7469 3
05947626 190	PreciControl ClinChem Multi 1 (4 × 5 mL)	System-ID 07 7469 3
05117216 190	PreciControl ClinChem Multi 2 (20 × 5 mL)	System-ID 07 7470 7
05947774 190	PreciControl ClinChem Multi 2 (4 × 5 mL)	System-ID 07 7470 7

English

System information

Test UREL, test ID 0-003 for serum and plasma

Test URELU, test ID 0-004 for urine

Intended use

In vitro test for the quantitative determination of the urea/BUN (blood urea nitrogen) concentration in human serum, plasma, and urine on COBAS INTEGRA systems.

Summary¹

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.

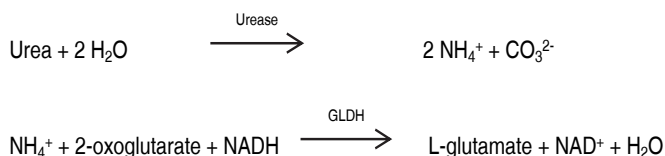
Determination of blood urea nitrogen is the most widely used screening test for renal function. When used in conjunction with serum creatinine determinations it can aid in the differential diagnosis of the three types of azotemia: prerenal, renal, and postrenal.

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. 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.



The rate of decrease in the NADH concentration is directly proportional to the urea concentration in the specimen. It is determined by measuring the absorbance at 340 nm.

Reagents - working solutions

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

R1 is in position B.

Precautions and warnings

Pay attention to all precautions and warnings listed in Section 1 / Introduction of this Method Manual.

Reagent handling

Ready for use

Storage and stability

Shelf life at 2-8 °C	See expiration date on cobas c pack label
COBAS INTEGRA 400 plus system	
On-board in use at 10-15 °C	8 weeks
COBAS INTEGRA 800 system	
On-board in use at 8 °C	8 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, EDTA or fluoride 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.

Stability in <i>serum/plasma</i> : ⁶	7 days at 15-25 °C
	7 days at 2-8 °C
	1 year at (-15)-(-25) °C

Stability in <i>urine</i> : ⁶	2 days at 15-25 °C
	7 days at 2-8 °C
	1 month at (-15)-(-25) °C

Materials provided

See "Reagents – working solutions" section for reagents.

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.

Application for serum, plasma and urine

COBAS INTEGRA 400 plus test definition

Measuring mode	Absorbance
Abs. calculation mode	Kinetic
Reaction direction	Decrease
Wavelength A/B	340/409 nm
Calc. first/last	23/28
Unit	mmol/L
<i>Serum, plasma</i>	
Reaction mode	R-S
<i>Urine</i>	
Reaction mode	D-R-S
Predilution factor	50

Pipetting parameters

<i>Serum/plasma/urine</i>	Diluent (H ₂ O)	
R	50 µL	95 µL
Sample	2 µL	98 µL
Total volume	245 µL	

COBAS INTEGRA 800 test definition

Measuring mode	Absorbance
Abs. calculation mode	Kinetic
Reaction direction	Decrease
Wavelength A/B	340/409 nm
Calc. first/last	27/36
Unit	mmol/L
<i>Serum, plasma</i>	
Reaction mode	R-S
<i>Urine</i>	
Reaction mode	D-R-S
Predilution factor	50

Pipetting parameters

<i>Serum/plasma/urine</i>	Diluent (H ₂ O)	
R	50 µL	150 µL
Sample	2 µL	43 µL
Total volume	245 µL	

Calibration

Calibrator	Calibrator f.a.s.
	Use deionized water as zero calibrator.
Calibration mode	Linear regression

Calibration replicate	Duplicate recommended
Calibration interval	Each cobas c pack, every 4 weeks, and as required following quality control procedures

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

Quality control

Quality control serum, plasma	Precinorm U, Precinorm U plus or PreciControl ClinChem Multi 1
	Precipath U, Precipath U plus or PreciControl ClinChem Multi 2
Quality control urine	Quantitative urine controls are recommended for routine quality control.
Control interval	24 hours recommended
Control sequence	User defined
Control after calibration	Recommended

For quality control, use control materials 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

COBAS INTEGRA analyzers automatically calculate the analyte concentration of each sample. For more details, please refer to Data Analysis in the Online Help (COBAS INTEGRA 400 plus/800 analyzers).

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.

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). Hemolytic specimens may cause high absorbance flagging. Choose diluted sample treatment for automatic rerun.

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.

Lipemic specimens may cause high absorbance flagging. Choose diluted sample treatment for automatic rerun.

Anticoagulants: Do not use ammonium heparin as an anticoagulant.

Therapeutic drug interference was tested according to the recommendations of the VDGH⁹. No interferences were found.

Ammonium ions may cause erroneously elevated results.

In very rare cases, gammopathy, in particular type IgM (Waldenström's macroglobulinemia), may cause unreliable results.⁸

For diagnostic purposes, the results should always be assessed in conjunction with the patient's medical history, clinical examination and other findings.

a) Verband der Diagnostica und Diagnostica Geräte Hersteller. Refer to section A of the Method Manual for a list of drugs tested and their concentrations.

ACTION REQUIRED

Special Wash Programming: The use of special wash steps is mandatory when certain test combinations are run together on COBAS INTEGRA analyzers. Refer to the CLEAN Method Sheet for further instructions and for the latest version of the Extra wash cycle list.

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, 1.4-112 mg/dL urea nitrogen)

Determine samples having higher concentrations via the rerun function. Dilution of samples via the rerun function is a 1:10 dilution. Results from samples diluted using the rerun function are automatically multiplied by a factor of 10.

Urine

1.0-2000 mmol/L (0.006-12 g/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.

Determine samples having lower concentrations via the rerun function. For samples with concentrations lower than 40 mmol/L, the rerun function reduces the sample predilution factor to 2 (final dilution 1 + 1 at COBAS INTEGRA 400 plus analyzers) or to 1 (undiluted at COBAS INTEGRA 800 analyzers). The results are automatically multiplied by the reduced predilution factor.

Lower limits of measurement

Serum/plasma

Lower detection limit of the test:

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 a zero sample (zero sample + 3 SD, repeatability, n = 30).

Urine

Lower detection limit of the test:

1.0 mmol/L (0.006 g/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 a zero sample (zero sample + 3 SD, repeatability, n = 30).

Expected values

Urea

Serum, plasma⁹

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

Urine¹⁰

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)^{b)}

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

Urea nitrogen (BUN)

Serum/plasma¹⁰

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)

Urine¹⁰

24-hour urine: 428-714 mmol/24 h (12-20 g/24 h),
corresponding to
286-595 mmol/L (801-1666 mg/dL)^{c)}

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

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 INTEGRA 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 and intermediate precision (2 aliquots per run, 2 runs per day, 20 days). The following results were obtained:

Serum/plasma

	Level 1	Level 2
Mean	4.08 mmol/L (24.6 mg/dL)	31.0 mmol/L (186 mg/dL)
CV repeatability	2.3 %	0.9 %
CV intermediate precision	3.9 %	2.8 %

Urine

	Level 1	Level 2
Mean	421 mmol/L (2.53 g/dL)	679 mmol/L (4.08 g/dL)
CV repeatability	1.3 %	1.2 %
CV intermediate precision	1.8 %	1.8 %

Method comparison

Serum/plasma

Urea values for human serum and plasma samples obtained on a COBAS INTEGRA 700 analyzer using the COBAS INTEGRA Urea/BUN reagent (y) were compared with those determined using commercially available reagents for urea on a COBAS INTEGRA 700 analyzer (x) and an alternative manufacturer's clinical chemistry system (x). Samples were measured in duplicate. Sample size (n) represents all replicates.

COBAS INTEGRA 700 analyzer

Sample size	(n)	236
Corr. coefficient	(r)	0.999
	(r _s)	0.999
Linear regression	y = 1.004x + 0.071 mmol/L	
Passing/Bablok ¹¹	y = 1.001x + 0.014 mmol/L	

Alternative system

Sample size	(n)	236
Corr. coefficient	(r)	0.999
	(r _s)	0.999
Linear regression	y = 0.983x + 0.176 mmol/L	
Passing/Bablok ¹¹	y = 0.995x + 0.041 mmol/L	

The sample concentrations were between 1.1 and 38.1 mmol/L (6.61 and 229 mg/dL).

Urine

Urea values for human urine samples obtained on a COBAS INTEGRA 700 analyzer using the COBAS INTEGRA Urea/BUN reagent (y) were compared with those determined using commercially available reagents for urea on a COBAS INTEGRA 700 analyzer (x).

UREAL

Urea/BUN

COBAS INTEGRA 700 analyzer

Sample size	(n)	120
Corr. coefficient	(r)	0.999
	(r _s)	0.998

Linear regression $y = 1.000x + 1.30 \text{ mmol/L}$ Passing/Bablok¹¹ $y = 0.999x + 3.47 \text{ mmol/L}$

The sample concentrations were between 56.6 and 796 mmol/L (0.340 and 4.78 g/dL).

References

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- 3 Talke H, Schubert GA. Enzymatische Harnstoffbestimmung in Blut und Serum im optischen Test nach Warburg. Klin Wochenschr 1965;43:174.
- 4 Tiffany TO, Jansen JM, Burtis CA, et al. Enzymatic kinetic rate and end-point analyses of substrate, by use of a GeMSAEC Fast Analyzer. Clin Chem 1972;18:829-840.
- 5 Sampson EJ, Baired MA, Burtis CA, et al. A coupled-enzyme equilibrium method for measuring urea in serum: Optimization and evaluation of the AACC study group on urea candidate reference method. Clin Chem 1980;26:816-826.
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- 10 Wu AHB, ed. Tietz Clinical Guide to Laboratory Tests, 4th edition. St. Louis (MO): Saunders Elsevier 2006;1096.
- 11 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

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Substrates



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