Application Sheet

Laboratory Name
Test Name: Urea/BUN

System information

For **cobas c** 501 analyzer:
UREAL: ACN 418 (serum/plasma/urine)
U-BUN: ACN 421 (serum/plasma/urine)
SUREA: ACN 419 (STAT, reaction time: 4, serum/plasma/urine)
SUBUN: ACN 427 (STAT, reaction time: 4, serum/plasma/urine)

Intended use

In vitro test for the quantitative determination of urea/urea nitrogen in human serum and plasma 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 %

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 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: For prescription use only.

Reagent handling

Ready for use

Storage and stability

UREAL

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. 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

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

In addition, other suitable control material can be used.

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 501 **test definition**

Assay type		Rate A	
Reaction time / Assay points		10 / 16-28 (STAT 4 / 16-28)	
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	
R2	38 µL	110 µL	
Sample volumes	*Sample*	*Sample dilution*	
		Sample	*Diluent (NaCl)*
Normal	2 µL	–	–
Decreased	6 µL	15 µL	120 µL
Increased	2 µL	–	–

Calibration

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

Traceability: This method has been standardized against SRM[a)] 912.

a) Standard Reference Method

Quality control

At least once daily run solutions at two levels of a quality control material with known concentrations.

Refer to Brown Clinic Quality Control Requirements, Rules and Reviews Policy
Refer to Brown Clinic Quatliy Control Specialty and Subspecialty Policy

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Calculation

Roche/Hitachi **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/dL urea nitrogen
mmol/L urea nitrogen x 0.02801 = g/L urea nitrogen
mg/dL urea x 0.467 = mg/dL 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).
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: 60 mg/dL or 1026 µmol/L).
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]

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
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 using the rerun function are automatically multiplied by a factor of 3.
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).

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)

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

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

For Known Interfering Substances section refer to package insert.
For Known Non-Interfering Substance refer to package insert.
For Additional Technical Information refer to package insert.

References

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Alternative method

Refer to Brown Clinic Back-up Testing Policy

Source document

Reagent Name: UREAL
Method Sheet Version: V7.0 English

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	Roche/Hitachi **cobas c** 311, **cobas c** 501/502
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	
04489357 190	Diluent NaCl 9 % (50 mL)	System-ID 07 6869 3	

Effective date

Effective date for this procedure:

Author

Source documentation compiled by Roche Diagnostics

Revised by: Heather J Hall, MBA, MT(ASCP), CG(ASCP)^{cm} Date: 4/9/2018

Approved by: Aaron Shives MD (Signature on file Date: 4/11/2018

REVIEW – REVISION SUMMARY DOCUMENTATION

Date: By: Revision Summary: