BECKMAN COULTER CE

AU

# Instructions For Use



# UREA
# UREA

REF OSR6134 4 x 25 mL R1, 4 x 25 mL R2
OSR6234 4 x 53 mL R1, 4 x 53 mL R2
OSR6634 4 x 173 mL R1, 4 x 173 mL R2

**For *in vitro* diagnostic use only.**

**ANNUAL REVIEW**

| Reviewed by | Date | Reviewed by | Date |
|---|---|---|---|
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| | | | |

## PRINCIPLE

### INTENDED USE

Kinetic UV test for the quantitative determination of urea in human serum, plasma and urine on Beckman Coulter analysers.

OSR6634 for use on the AU5800, AU2700 and AU5400 systems only.

### SUMMARY AND EXPLANATION

Reference[1,2]

Urea is synthesised in the liver as the final product of protein and amino acid metabolism. Urea synthesis is therefore dependant on daily protein intake and endogenous protein metabolism. Most of the urea produced during these metabolic processes is eliminated by glomerular filtration, with 40 – 60% diffusing back into the blood, irrespective of the flow rate in the proximal tubule. Rediffusion in the distal tubule depends on the urinary flow and is regulated by antidiuretic hormone. During diuresis, there is minimal rediffusion of urea into the blood; a large quantity of urea is excreted in the urine and plasma urea concentration is low.

During antidiuresis, which may occur in oliguric heart failure, exsiccosis or thirst, urea rediffuses in the tubules at an increased rate and plasma urea is increased. In pre- and post renal kidney failure, the tubular urine flow is decreased, resulting in increased rediffusion of urea in the distal tubules and increased creatinine secretion. Prerenal elevation of urea occurs in cardiac decompensation, increased protein catabolism and water depletion. Urea levels may be elevated due to renal causes such as acute glomerulonephritis, chronic nephritis, polycystic kidney, tubular necrosis and nephrosclerosis. Post renal elevation of urea may be caused by obstruction of the urinary tract.

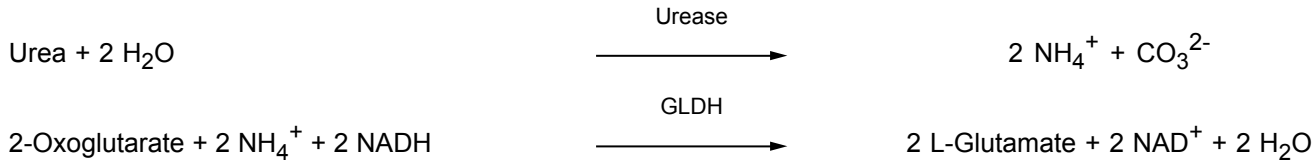
Plasma urea concentration is determined by renal perfusion, urea synthesis rate, and glomerular filtration rate (GFR) and may be increased in acute renal failure, chronic renal failure and prerenal azotaemia. In dialysis patients the urea concentration is representative of protein degradation and is also an indicator of metabolic status. In end-stage renal failure, the urotoxic signs, in particular those relating to the gastrointestinal system, correlate well with urea concentration. Serum urea and serum creatinine determinations are frequently performed together in the differential diagnosis of kidney function.

### METHODOLOGY

Reference[3]

Urea is hydrolysed in the presence of water and urease to produce ammonia and carbon dioxide. The ammonia produced in the first reaction combines with 2-oxoglutarate and NADH in the presence of glutamate-dehydrogenase (GLDH) to yield glutamate and $NAD^+$. The decrease in NADH absorbance per unit time is proportional to the urea concentration.

### CHEMICAL REACTION SCHEME




## SPECIMEN

### TYPE OF SPECIMEN

Serum and EDTA or lithium heparinised plasma. Do not use ammonium heparinised plasma.[1]

Stable in serum and plasma for 7 days when stored at 2…25°C.[4]

Strongly icteric samples should be avoided.

Urine: 24-hour collection without preservatives is recommended.[5]

Stable in urine for 7 days when stored at 2…8°C and 2 days when stored at 15…25°C.[4]

Specimen storage and stability information provides guidance to the laboratory. Based on specific needs, each laboratory may establish alternative storage and stability information according to good laboratory practice or from alternative reference documentation.

## REAGENTS

### WARNING AND PRECAUTIONS

Exercise the normal precautions required for handling all laboratory reagents.

Dispose of all waste material in accordance with local guidelines.

This product contains material of animal origin. The product should be considered as potentially capable of transmitting infectious diseases.

### REACTIVE INGREDIENTS

Final concentration of reactive ingredients:

| | |
|---|---|
| Tris buffer | 100 mmol/L |
| NADH | ≥ 0.26 mmol/L |
| Tetra-Sodium diphosphate | 10 mmol/L |
| EDTA | 2.65 mmol/L |
| 2-Oxoglutarate | ≥ 9.8 mmol/L |

| | |
|---|---|
| Urease | ≥ 17.76 kU/L |
| ADP | ≥ 2.6 mmol/L |
| GLDH | ≥ 0.16 kU/L |
| Preservative | |

The concentrations of the reactive components of the reagents shown on the kit label are the actual concentrations in the individual R1/R2 vials. The reagent composition which is shown in the Instructions For Use is the final concentration of these components in the reaction cuvette after addition of R1, Sample, and R2.

> ⚠ **CAUTION**
>
> **Sodium azide preservative may form explosive compounds in metal drain lines. See NIOSH Bulletin: Explosive Azide Hazard (8/16/76).**
> **To avoid the possible build-up of azide compounds, flush wastepipes with water after the disposal of undiluted reagent. Sodium azide disposal must be in accordance with appropriate local regulations.**

### GHS HAZARD CLASSIFICATION

| | | |
|---|---|---|
| (UREA R1 ) | EUH208 | May produce an allergic reaction. |
| | | reaction mass of: 5-chloro-2-methyl-4-isothiazolin -3-one [EC# 247-500-7] and 2-methyl-4-isothiazolin-3-one [EC# 220-239-6](3:1) < 0.05% |
| (UREA R2 ) | WARNING | |
| | H316 | Causes mild skin irritation. |
| | P332+P313 | If skin irritation occurs: Get medical advice/attention. |
| | | Sodium Pyrophosphate, Decahydrate 1 - 2% |
| | | Tris(hydroxymethyl)– aminomethane 2 - 5% |

| | |
|---|---|
| SDS | Safety Data Sheet is available at techdocs.beckmancoulter.com |

### REAGENT PREPARATION

The reagents are ready for use and can be placed directly on board the instrument

### STORAGE AND STABILITY

The reagents are stable, unopened, up to the stated expiry date when stored at 2…8°C. Once open, reagents stored on board the instrument are stable for 30 days.

## CALIBRATION

### CALIBRATOR REQUIRED

Use System Calibrator Cat. No. 66300 for serum and plasma application and Urine Calibrator Cat. No. B64606 for urine application.

The urea values of System Calibrator Cat. No. 66300 are traceable to the National Institute of Standards and Technology (NIST) Reference Material (SRM) 909b Level 1. The urea values of the Urine Calibrator Cat. No. B64606 are traceable to the National Institute of Standards and Technology (NIST) Reference Material (SRM) 912a.

Recalibrate the assay when the following occur:

Change in reagent lot or significant shift in control values;

Major preventative maintenance was performed on the analyser or a critical part was replaced.

## QUALITY CONTROL

Controls Cat. No. ODC0003 and ODC0004 or other control materials with values determined by this Beckman Coulter system may be used for the serum/plasma application.

Biorad Liquichek Urine Chemistry Controls Cat. No. 397 and 398 or other control materials with values determined by this Beckman Coulter system may be used for the urine application.

Each laboratory should establish its own control frequency however good laboratory practice suggests that controls be tested each day patient samples are tested and each time calibration/blanking is performed.

The results obtained by any individual laboratory may vary from the given mean value. It is therefore recommended that each laboratory generates analyte specific control target values and intervals based on multiple runs according to their requirements. These target values should fall within the corresponding acceptable ranges given in the relevant product literature.

If any trends or sudden shifts in values are detected, review all operating parameters.

Each laboratory should establish guidelines for corrective action to be taken if controls do not recover within the specified limits.

## TESTING PROCEDURE(S)

Refer to the appropriate Beckman Coulter AU analyser User Guide/Instructions For Use (IFU) for analyser-specific assay instructions for the sample type as listed in the Intended Use statement. The paediatric application is suitable for use with small volume serum/plasma samples.

## CALCULATIONS

The Beckman Coulter analysers automatically compute the urea concentration of each sample.

## REPORTING RESULTS

### REFERENCE INTERVALS

| | |
|---|---|
| Serum/Plasma Adult (Global)[1] | 2.8 – 7.2 mmol/L (17 – 43 mg/dL) |
| Newborn[6] | 1.4 – 4.3 mmol/L (8.4 – 25.8 mg/dL) |
| Infant/child | 1.8 – 6.4 mmol/L (10.8 – 38.4 mg/dL) |
| Urine[7] | 250 – 570 mmol/day (15,000 – 34,200 mg/day) |

Expected values may vary with age, sex, sample type, diet and geographical location. Each laboratory should verify the transferability of the expected values to its own population, and if necessary determine its own reference interval according to good laboratory practice. For diagnostic purposes, results should always be assessed in conjunction with the patient's medical history, clinical examinations and other findings.

# PROCEDURAL NOTES

### LIMITATIONS

Highly lipemic samples may exceed the reaction absorbance and will be flagged with a "@". Such samples should be diluted and re-run.

Reliable estimations of Urea can only be achieved if steps are taken to avoid contamination from Ammonia. Reagents on the carousel which contain/liberate Ammonia may contaminate Urea OSR6x34 . Avoid the use of ammonia containing reagents (e.g Paracetamol OSR6x202) together with Urea to mitigate against atmospheric ammonia transfer. Please be advised that atmospheric ammonia may also be released by the use of certain laboratory cleaning products. Please contact your local Beckman Coulter representative for further information.

### INTERFERENCES

Results of serum studies conducted to evaluate the susceptibility of the method to interference were as follows:

| | |
|---|---|
| Icterus: | Interference less than 10% up to 20 mg/dL or 342 µmol/L bilirubin |
| Haemolysis: | Interference less than 10% up to 2.5 g/L haemoglobin |
| Lipemia: | Interference less than 3% up to 500 mg/dL Intralipid |

Results of urine studies conducted to evaluate the susceptibility of the method to interference were as follows:

| | |
|---|---|
| Icterus: | Interference less than 3% up to 40 mg/dL or 684 µmol/L bilirubin |
| Haemolysis: | Interference less than 3% up to 5 g/L haemoglobin |

Refer to Young[8] for further information on interfering substances.

# PERFORMANCE CHARACTERISTICS

### PERFORMANCE CHARACTERISTICS

Data contained within this section is representative of performance on Beckman Coulter systems. Data obtained in your laboratory may differ from these values.

### LINEARITY

The test is linear within a concentration range of 0.8 – 50 mmol/L (5 – 300 mg/dL) for serum and plasma.

The test is linear within a concentration range of 10 – 750 mmol/L (60 – 4,500 mg/dL) for urine.

### SENSITIVITY

The lowest detectable level using serum settings on an AU5800 analyser was estimated at 0.11 mmol/L.

The lowest detectable level using urine settings on the AU2700 was estimated as 5.71 mmol/L.

The lowest detectable level represents the lowest measurable level of urea that can be distinguished from zero. It is calculated as the absolute mean plus three standard deviations of 20 replicates of an analyte free sample.

### METHODS COMPARISON

Patient serum samples were used to compare this Urea OSR6134 assay on the AU600 against another commercially available urea assay. Results of linear regression analysis were as follows:

| | | | |
|---|---|---|---|
| y = 0.928x - 0.206 | r = 0.999 | n = 116 | Sample range = 1.38 – 39.44 mmol/L |

Patient urine samples were used to compare this Urea OSR6134 assay on the AU2700 against another commercially available urea assay. Results of linear regression analysis were as follows:

| | | | |
|---|---|---|---|
| y = 0.976x - 2.144 | r = 0.999 | n = 125 | Sample range = 46.05 – 683.55 mmol/L |

**PRECISION**

The following data was obtained on an AU640 using 3 serum pools analysed over 20 days.

| **n = 80** | **Within-run** | | **Total** | |
|---|---|---|---|---|
| **Mean mmol/L** | **SD** | **CV%** | **SD** | **% CV** |
| 1.97 | 0.05 | 2.28 | 0.06 | 3.25 |
| 9.71 | 0.10 | 1.03 | 0.23 | 2.38 |
| 37.40 | 0.34 | 0.91 | 0.91 | 2.42 |

The following data was obtained on an AU640 using 3 urine pools analysed over 20 days.

| **n = 80** | **Within-run** | | **Total** | |
|---|---|---|---|---|
| **Mean mmol/L** | **SD** | **CV%** | **SD** | **CV%** |
| 78.81 | 0.81 | 1.02 | 2.44 | 3.09 |
| 283.97 | 2.50 | 0.88 | 9.68 | 3.41 |
| 436.70 | 4.80 | 1.10 | 14.01 | 3.21 |

## ADDITIONAL INFORMATION

DxC 700 AU requires that each reagent application has a standard format of abbreviated Closed Test Name. This Closed Test Name is required to allow automated loading of the calibrator information for each application as part of the DxC 700 AU Closed System. Refer to the table below for the Closed Test Name assigned to each application for this assay.

| **Test Name** | **Description** |
|---|---|
| BUN1N | Urea/Urea Nitrogen (Serum) |
| BUN1N, BUN1NP | Urea/Urea Nitrogen (Urine) |
| BUN1NP | Urea/Urea Nitrogen (Serum Paediatric) |

**Setting Sheet Footnotes**

# User defined

Serum: † System Calibrator Cat. No.: 66300.

Urine: † Urine Calibrator Cat. No: B64606. Ensure relevant value sheet is used.

* Values set for working in SI units (mmol/L). To work in mg/dL multiply by 6.

Ω Depends on usage pattern in the laboratory.

** BUN1N to link with Serum Application, BUN1NP to link with Paediatric Serum Application

** Test Name ‘UREA’ to link with Paediatric Serum Application ‘UREAP’

**REVISION HISTORY**

Removed reference to obsolete calibrator.

**Preceding version revision history**

IFU updated to add Vietnamese language.

Revised GHS section

# REFERENCES


1. Thomas L. Urea and blood urea nitrogen (BUN). In:Thomas L, ed. Clinical laboratory diagnostics.Use and assessment of clinical laboratory results. Frankfurt/Main: TH-Books Verlagsgesellschaft, 1998:374-377.

2. Newman DJ, Price CP. Renal function and nitrogen metabolites. In: Burtis CA, Ashwood ER, eds. Tietz textbook of clinical chemistry. Philadelphia: WB Saunders Company, 1999;1239-1241.

3. Talke H, Schubert GE. Enzymatische harnstoffbestimmung in blut und serum im optischen test nach Warburg. Klin Wochenschr 1965;43:174-75.

4. Ehret W, Heil W, Schmitt Y, Töpfer G, Wisser H, Zawta B, et al. Use of anticoagulants in diagnostic laboratory investigations and stability of blood, plasma and serum samples. WHO/DIL/LAB/99.1 Rev.2:44pp, 49pp.

5. NCCLS. Urinalysis and collection, transportation, and preservation of urine specimens; approved guideline. NCCLS Document GP16-A2, 2nd ed. Pennsylvania: NCCLS, 2001.

6. Painter PC, Cope JY, Smith JL. Reference information for the clinical laboratory. In: Burtis CA, Ashwood ER, eds. Tietz textbook of clinical chemistry. Philadelphia:WB Saunders Company, 1999; 1838pp.

7. Kazmierczak. Urea. In: Kaplan LA, Pesce AJ, eds. Clinical chemistry theory, analysis and correlation. St. Louis: Mosby; 1996:500pp.

8. Young DS. Effects of drugs on clinical laboratory tests, 5$^{th}$ed. AACC Press, 2000.



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