BECKMAN COULTER CE

AU

Instructions For Use

UA
URIC ACID

REF OSR6098 4 x 12 mL R1, 4 x 5 mL R2
OSR6198 4 x 30 mL R1, 4 x 12.5 mL R2
OSR6298 4 x 42.3 mL R1, 4 x 17.7 mL R2
OSR6698 4 x 124 mL R1, 4 x 55 mL R2

For *in vitro* diagnostic use only.

ANNUAL REVIEW

Reviewed by	Date	Reviewed by	Date

PRINCIPLE

INTENDED USE

Enzymatic colour test for the quantitative determination of uric acid in human serum, plasma and urine on Beckman Coulter analysers.

OSR6698 for use on the AU5800, AU2700 and AU5400 systems only.

SUMMARY AND EXPLANATION

Reference[1,2]

Uric Acid is the major product of purine catabolism in humans. Most uric acid formation occurs in the liver, and is eliminated via the kidney, with the body uric acid pool determined by the balance between synthesis and elimination. Hyperuricaemia is divided into primary and secondary classifications, involving either overproduction or reduced elimination. Primary hyperuricaemia is also known as the idiopathic or familial form. In the vast majority of affected cases, reduced tubular secretion of uric acid is responsible for the elevation in uric acid levels. Approximately 1% of patients with primary hyperuricaemia have an enzymatic defect in purine metabolism which results in overproduction of uric acid. Primary hyperuricaemia is associated with gout, Lesch-Nyhan syndrome, Kelley Seegmiller syndrome and increased phosphoribosyl pyrophosphate synthase activity. Secondary hyperuricaemia may be caused by increased nutritional purine uptake, associated with increased uric acid excretion in the urine. Secondary hyperuricaemia is associated with numerous conditions including renal insufficiency, myeloproliferative diseases, haemolytic diseases, psoriasis, polycythemia vera, type I glycogen storage disease, excess alcohol consumption, lead intoxication, a purine-rich diet, fasting, starvation and chemotherapy.

Hypouricaemia may result from decreased uric acid production, such as occurs in hereditary xanthinuria, hereditary purine nucleoside phosphorylase deficiency and allopurinol therapy. Hypouricaemia may also be due to increased renal uric acid excretion, which may occur in malignant diseases, AIDS, Fanconi syndrome, diabetes mellitus, severe burns and hypereosinophilic syndrome. In addition, hypouricaemia may result from treatment with uricosuric agents and ingestion of X-ray contrast media. Quantitation of urinary uric acid excretion may assist in the selection of appropriate

treatment for hyperuricaemia, providing an indication of whether patients should be treated with uricosuric drugs to enhance renal excretion, or allopurinol to supress purine synthesis.

METHODOLOGY

Reference[3]

Uric acid is converted by uricase to allantoin and hydrogen peroxide. The Trinder reaction is utilised to measure H_2O_2. The formed H_2O_2 reacts with N,N-bis(4-sulfobutyl)-3,5-dimethylaniline, disodium salt (MADB) and 4-aminophenazone in the presence of peroxidase to produce a chromophore, which is read biochromatically at 660/800nm. The amount of dye formed is proportional to the uric acid concentration in the sample.

CHEMICAL REACTION SCHEME

$$\text{Uric acid} + O_2 + 2\,H_2O \xrightarrow{\text{Uricase}} \text{Allantoin} + CO_2 + H_2O_2$$

$$2\,H_2O_2 + \text{MADB} + \text{4-Aminophenazone} \xrightarrow{\text{Peroxidase}} \text{Blue dye}^+ + OH^- + 3\,H_2O$$

SPECIMEN

TYPE OF SPECIMEN

Reference[4,5]

Serum and EDTA or heparinised plasma.

Stable in serum and plasma for 7 days when stored at 2…8°C and 3 days when stored at 15…25°C.

Urine: Stable in urine for 4 days when stored at 15…25°C. To prevent urate precipitation in urine specimens after collection, add a sufficient volume of sodium hydroxide to bring the pH between 8 and 9.

EDTA plasma will give a 5 – 10% lower recovery compared to serum or heparinised plasma.

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 active ingredients:

Phosphate Buffer (pH 7.5)	42 mmol/L
MADB	0.15 mmol/L
4-Aminophenazone	0.30 mmol/L
Peroxidase	≥ 5.9 kU/L (98 µkat/L)

Uricase	≥ 0.25 kU/L (4.15 µkat/L)
Ascorbate Oxidase	≥ 1.56 kU/L (26 µkat/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

URIC ACID R1 — WARNING

H317	May cause an allergic skin reaction.
H412	Harmful to aquatic life with long lasting effects.
P273	Avoid release to the environment.
P280	Wear protective gloves, protective clothing and eye/face protection.
P333+P313	If skin irritation or rash occurs: Get medical advice/attention.
P362+P364	Take off contaminated clothing and wash it before use.
	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%

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 uric acid values of System Calibrator Cat. No. 66300 are traceable to the Isotope Dilution Mass Spectrometry Reference Method (IDMS). The uric acid values of the Urine Calibrator Cat. No. B64606 are traceable to the National Institute of Standards and Technology (NIST) Reference Material (SRM) 913b.

Recalibrate the assay every 30 days, or when the following occur:

Change in reagent lot number 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 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.

CALCULATIONS

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

REPORTING RESULTS

REFERENCE INTERVALS

Reference[6]		
Serum	Male	208.3 – 428.4 µmol/L (3.5 – 7.2 mg/dL)
	Female	154.7 – 357.0 µmol/L (2.6 – 6.0 mg/dL)
Urine, 24h	Average diet	1488 – 4463 µmol/d (250 – 750 mg/d)

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

INTERFERENCES

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

Ascorbate :	Interference less than 5% up to 20 mg/dL ascorbate.
Icterus:	Interference less than 5% up to 40 mg/dL or 684 µmol/L unconjugated bilirubin.
	Interference less than 10% up to 20 mg/dL or 342 µmol/L conjugated bilirubin.
Haemolysis:	Interference less than 5% up to 5 g/L haemoglobin.
Lipemia:	Interference less than 5% up to 1,000 mg/dL Intralipid. (AU480 Interference less than 10% up to 1,000 mg/dL Intralipid.)

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

Ascorbate :	Interference less than 5% up to 50 mg/dL ascorbate.

Patients treated with N-Acetyl Cysteine (NAC) for a Paracetamol overdose may generate a false low result for uric acid.

In very rare cases gammopathy, especially IgM (Waldenström's macroglobulinemia), may cause unreliable results.

Venipuncture immediately after or during the administration of Metamizole (Dipyrone) may lead to falsely low results for Uric Acid. Venipuncture should be performed prior to the administration of Metamizole.

N-acetyl-p-benzoquinone imine (metabolite of Paracetamol) will generate erroneously low results in samples for patients that have taken toxic doses of paracetamol.

Refer to Young[7] for further information on interfering substances.

PERFORMANCE CHARACTERISTICS

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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 89 – 1,785 µmol/L (1.5 – 30 mg/dL) for serum and plasma. The test is linear within a concentration range of 119 – 23,800 µmol/L (2 – 400 mg/dL) for urine.

SENSITIVITY

The lowest detectable level using serum settings on an AU2700 analyser was estimated at 2 µmol/L.

The lowest detectable level using urine settings on an AU640 analyser was estimated at 10 µmol/L.

The lowest detectable level represents the lowest measurable level of uric acid 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 samples were used to compare this uric acid assay on the AU640 against another commercially available uric acid assay. Results of linear regression analysis were as follows:

Serum Samples:

y = 0.964x – 12.498	r = 0.999	n = 116	Sample range = 94 – 1,531 µmol/L

Urine Samples:

y = 0.982x + 80.76	r = 1.000	n = 151	Sample range = 142 – 20,653 µmol/L

PRECISION

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

n = 80	**Within-run**		**Total**	
Mean µmol/L	**SD**	**CV%**	**SD**	**CV%**
171.84	1.91	1.11	2.94	1.71
388.23	6.02	1.55	9.48	2.44
1362.06	9.90	0.73	28.86	2.12

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

n = 80	**Within-run**		**Total**	
Mean µmol/L	**SD**	**CV%**	**SD**	**CV%**
1360.16	14.39	1.06	22.63	1.66
3660.61	57.57	1.57	71.24	1.95
5604.48	98.50	1.76	93.44	1.67

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**
UA-1N	Uric Acid (Serum)
UA-1N	Uric Acid (Urine)

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 (µmol/L). To work in mg/dL divide by 59.5.

REVISION HISTORY

Revised GHS section

Preceding version revision history

Removed reference to obsolete calibrator.

REFERENCES

1. Thomas L. Uric acid. In: Thomas L, Hrsg. Labor und Diagnose. Indikation und Bewertung von Laborbefunden für die medizinische Diagnostik. Frankfurt/Main: TH-Books Verlagsgesellschaft, 2005:280-289.

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;1245-50.

3. Barham D, Trinder P. An improved colour reagent for the determination of blood glucose by the oxidase system. Analyst 1972;97:142-5.

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. In-house data on file.

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. Young DS, Effects of Drugs on CLINICAL Laboratory Tests, AACC, 5th ed. CCPress, 2000.

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