BECKMAN COULTER CE

AU

Instructions For Use

CREA
CREATININE

REF OSR6178 4 x 51 mL R1, 4 x 51 mL R2
OSR6678 4 x 173 mL R1, 4 x 173 mL R2

For *in vitro* diagnostic use only.

ANNUAL REVIEW

Reviewed by	Date	Reviewed by	Date

PRINCIPLE

INTENDED USE

Kinetic colour test (Jaffé method) for the quantitative determination of creatinine in human serum, plasma and urine on Beckman Coulter AU analysers. The OSR6x78 reagents may be used in two ways for the serum application:

Method A : Kinetic Jaffe (compensated method) traceable to the IDMS reference method.

Method B : Kinetic Jaffe uncompensated.

OSR6678 for use on the AU5800, AU2700 and AU5400 systems only.

SUMMARY AND EXPLANATION

Reference[1,2,3]

Creatinine is a metabolic product of creatine and phosphocreatine, which are both found almost exclusively in muscle. Thus, creatinine production is proportional to muscle mass and varies little from day to day.

Measurements of creatinine are used in the diagnosis and treatment of renal disease and prove useful in the evaluation of kidney glomerular function and in monitoring renal dialysis. However, the serum level is not sensitive to early renal damage and responds more slowly than blood urea nitrogen (BUN) to haemodialysis during treatment of renal failure. Both serum creatinine and BUN are used to differentiate prerenal and postrenal (obstructive) azotemia. An increase in serum BUN without concomitant increase of serum creatinine is key to identifying prerenal azotemia. In post renal conditions where obstruction to the flow of urine is present e.g. malignancy, nephrolithiasis and prostatism, both the plasma creatinine and urea levels will be increased; in these situations the rise is disproportionately greater for BUN due to the increased back diffusion of urea.

Serum creatinine varies with the subject's age, body weight, and sex. It is sometimes low in subjects with relatively small muscle mass, cachectic patients, amputees, and in older persons. A serum creatinine level that would usually be considered normal does not rule out the presence of impaired renal function.

METHODOLOGY

Reference[4, 5, 6]

Creatinine forms a yellow-orange coloured compound with picric acid in an alkaline medium. The rate of change in absorbance at 520/800 nm is proportional to the creatinine concentration in the sample.

CHEMICAL REACTION SCHEME

Creatinine + picric acid ⟶ Creatinine picrate complex

SPECIMEN

TYPE OF SPECIMEN

Serum and EDTA or heparinised plasma.

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

Strongly lipemic samples should be avoided.

Urine: Collect urine without using preservatives. Store at 2…8°C.[8]

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.

REACTIVE INGREDIENTS

Final concentration of reactive ingredients:

Sodium hydroxide	120 mmol/L
Picric acid	2.9 mmol/L

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.

GHS HAZARD CLASSIFICATION

Creatinine R1	DANGER	
		
	H314	Causes severe skin burns and eye damage.
	P280	Wear protective gloves, protective clothing and eye/face protection.
	P301+P330+P331	IF SWALLOWED: rinse mouth. Do NOT induce vomiting.
	P303+P361+P353	IF ON SKIN (or hair): Rinse skin with water.
	P305+P351+P338	IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.
	P310	Immediately call a POISON CENTER or doctor/physician.
		Sodium Hydroxide 0.5 - 1%
Creatinine R2	DANGER	
		
	H314	Causes severe skin burns and eye damage.
	P280	Wear protective gloves, protective clothing and eye/face protection.
	P301+P330+P331	IF SWALLOWED: rinse mouth. Do NOT induce vomiting.
	P303+P361+P353	IF ON SKIN (or hair): Rinse skin with water.
	P305+P351+P338	IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.
	P310	Immediately call a POISON CENTER or doctor/physician.
		Picric Acid 0.1 - 0.5%

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, protected from light, unopened, up to the stated expiry date when stored at 2…8°C. Once open, reagents stored on board the instrument are stable for 7 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 serum calibrator creatinine value for method A is traceable to the Isotope Dilution Mass Spectroscopy (IDMS) method via National Institute of Standards and Technology (NIST) Standard Reference Material (SRM) 967.

The serum calibrator creatinine value for method B is traceable to the National Institute of Standards and Technology (NIST) Standard Reference Material (SRM) 909b Level 2.

The urine calibrator B64606 creatinine value is traceable to NIST SRM 3667.

Calibrate the reagent on a daily basis and run QC at a minimum of every 8 hours as part of your laboratory's quality control program. Recalibrate the reagent when there is a drift in QC recovery outside of your laboratory's acceptance limits.

Recalibrate when the following occur:

Change in reagent bottle or significant shift in control values;

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

Absorption of atmospheric CO_2 by the reagent on board the analyser can impair calibration stability. This effect will vary depending upon the rate of use.

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.

Run QC at a minimum of every 8 hours. Recalibrate the reagent when there is a drift in QC recovery outside of your laboratory's acceptance limits.

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.

The effect of the atmospheric CO_2 uptake by the reagent on board the analyser is more pronounced as the volume in the reagent vial is reduced.

TESTING PROCEDURE(S)

Two distinct test procedures are available for the serum application of this reagent:

A:

Interference from protein is mathematically corrected by subtracting 18 µmol/L from each test result (Specific Test Parameters: Correlation factor B = -18).

B:

Uncompensated Jaffe (no protein compensation, B = 0)

Both methods require different calibrator set points and deliver slightly different results for patients and control sera at low creatinine concentrations which results in different reference ranges.

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 creatinine concentration of each sample.

REPORTING RESULTS

REFERENCE INTERVALS

Method A (IDMS traceable)		Method B (Uncompensated Jaffe)	
Serum/Plasma[9,10]		Serum/Plasma[3,11]	
Male	59 – 104 µmol/L (0.67 – 1.17 mg/dL)	Male < 50 years	74 – 110 µmol/L (0.84 – 1.25 mg/dL)
Female	45 – 84 µmol/L (0.51 – 0.95 mg/dL)	Male >50 years	72 – 127 µmol/L (0.81 – 1.44 mg/dL)
Neonate	27 – 87 µmol/L (0.31 – 0.98 mg/dL)	Female	58 – 96 µmol/L (0.66 – 1.09 mg/dL)
Infant	14 – 34 µmol/L (0.16 – 0.39 mg/dL)	Neonate	45 – 105 µmol/L (0.5 – 1.2 mg/dL)
Child	23 – 68 µmol/L (0.26 – 0.77 mg/dL)	Infant	35 – 62 µmol/L (0.4 – 0.7 mg/dL)
		Child	45 – 105 µmol/L (0.5 – 1.2 mg/dL)
Urine[12]		Urine[12]	
Male	124 – 230 µmol/kg/d (14 – 26 mg/kg/d)	Male	124 – 230 µmol/kg/d (14 – 26 mg/kg/d)
Female	97 – 177 µmol/kg/d (11 – 20 mg/kg/d)	Female	97 – 177 µmol/kg/d (11 – 20 mg/kg/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 serum studies conducted to evaluate the susceptibility of the method to interference were as follows:

Icterus:	Interference less than 10% up to 40 mg/dL or 684 µmol/L bilirubin
Haemolysis:	Interference less than 3% up to 5 g/L haemoglobin
Lipemia:	Interference less than 10% up to 600 mg/dL Intralipid
Protein:	Interference less than 6% between 3 and 10 g/dL protein for method A
	Interference less than 20% between 3 and 12 g/dL protein for method B

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
Ascorbate :	Interference less than 3% up to 50 mg/dL ascorbate
Glucose:	Interference less than 3% up to 3,000 mg/dL glucose

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

Refer to Young[13] 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

Method A is linear within a concentration range of 5 – 2,200 µmol/L (0.06 – 25.0 mg/dL) for serum and plasma.

Method B is linear within a concentration range of 18 – 2,200 µmol/L (0.2 – 25.0 mg/dL) for serum and plasma.

The test is linear within a concentration range of 88 – 35,360 µmol/L (1 – 400 mg/dL) for urine.

SENSITIVITY

The lowest detectable level of method A using serum settings on a DxC 700 AU analyser was established at 0.98 µmol/L (0.011 mg/dL).

The lowest detectable level of method B using serum settings on a DxC 700 AU analyser was established at 1.53 µmol/L (0.017 mg/dL).

The lowest detectable level using urine settings on a DxC 700 AU analyser was established at 10.37 µmol/L (0.117 mg/dL).

The lowest detectable level represents the lowest measurable level of creatinine 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 Creatinine OSR6178 assay (method A) on the AU2700 against the Creatinine OSR6178 assay (method B). Results of linear regression analysis were as follows:

y = 1.04x – 17	r = 0.999	n = 701	Sample range = 26.5 – 1,024 µmol/L

Patient serum samples were used to compare this Creatinine OSR6178 assay (method A) on the AU2700 against a commercially available enzymatic creatinine assay which has demonstrated equivalence to the IDMS reference method. Results of linear regression analysis were as follows:

y = 1.01x + 2.8	r = 0.997	n = 701	Sample range = 13.3 – 1,007 µmol/L

Patient urine samples were used to compare this Creatinine OSR6178 assay on the AU2700 against another commercially available creatinine assay. Results of linear regression analysis were as follows:

y = 0.916x + 266.607	r = 0.998	n = 124	Sample range = 1,246 – 32,562 µmol/L

PRECISION

The following data was obtained on a DxC 700 AU using 3 serum pools analysed over 20 days.

n = 80	Within-run		Total	
Mean µmol/L	**SD**	**CV%**	**SD**	**CV%**
94.56	1.06	1.12	1.59	1.68
156.44	1.46	0.94	1.83	1.17
983.13	8.12	0.83	11.42	1.16

The following data was obtained on a DxC 700 AU using 3 urine pools analysed over 20 days.

n = 80	Within-run		Total	
Mean µmol/L	**SD**	**CV%**	**SD**	**CV%**
2,612	22.02	0.8	79.48	3.0
12,927	87.13	0.7	389.47	3.0
34,315	219.85	0.6	688.86	2.0

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
CRE2N	Creatinine - Method A (Serum)
CRE2N	Creatinine - Method A (Urine)
CRE1N	Creatinine - Method B (Serum)
CRE1N	Creatinine - Method B (Urine)
CRE2NP	Creatinine - Method A (Serum Paediatric)
CRE2NP	Creatinine - Method A (Urine Paediatric)
CRE1NP	Creatinine - Method B (Serum Paediatric)
CRE1NP	Creatinine - Method B (Urine Paediatric)

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 88.4.

‡ Calibrate daily and run QC at a minimum of every 8 hours. Recalibrate the reagent when there is a drift in QC recovery outside of your laboratory's acceptance limits.

^ Adjusted with B factor of -18

** CRE1N to link with Serum Application, CRE1NP to link with Paediatric Serum Application

** CRE2N to link with Serum Application, CRE2NP to link with Paediatric Serum Application

REVISION HISTORY

Updated Performance Characteristics section

Preceding version revision history

Removed reference to obsolete calibrator.

REFERENCES

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