BECKMAN COULTER CE

SYNCHRON System(s)

Chemistry Information Sheet

CR-E

Creatinine

REF A60298

For *In Vitro* Diagnostic Use

Rx Only

ANNUAL REVIEW

Reviewed by	Date	Reviewed by	Date

PRINCIPLE

INTENDED USE

CR-E reagent, when used in conjunction with UniCel® DxC System(s) and SYNCHRON® Systems AQUA CAL 1 and 2, is intended for the quantitative determination of creatinine (CR-E) concentration in human serum, plasma or urine.

CLINICAL SIGNIFICANCE

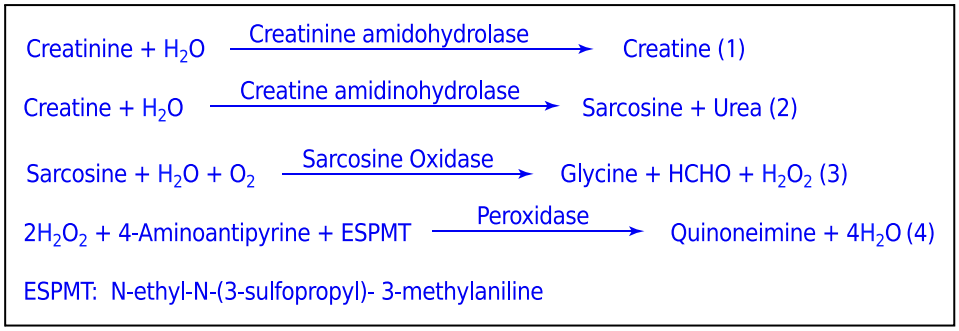
Creatinine measurements are used in the diagnosis and treatment of renal diseases, in monitoring renal dialysis, and as a calculation basis for measuring other urine analytes.

METHODOLOGY

CR-E reagent is used to measure the creatinine concentration by an enzymatic method.[1,2] This enzymatic creatinine method utilizes a multi-step approach ending with a photometric end-point reaction. The enzyme creatinine amidohydrolase is used to convert creatinine to creatine. Creatine is further broken down through a series of enzymatic reactions to yield a colored chromogen read at 560 nm.

The System(s) automatically dilutes urine samples and proportions the appropriate sample and reagent volumes into a cuvette. The ratio used is one part sample to 24 parts reagent for serum or plasma and one part diluted sample to 24 parts reagent for urine. The System monitors the change in absorbance at 560 nanometers. This change is directly proportional to the concentration of creatinine in the sample and used by the System to calculate and express CR-E concentration.

CHEMICAL REACTION SCHEME



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SPECIMEN

TYPE OF SPECIMEN

Biological fluid samples should be collected in the same manner routinely used for any laboratory test.[3] Freshly drawn serum, plasma or freshly collected urine (random/timed) are the specimens of choice. Acceptable anticoagulants are listed in the PROCEDURAL NOTES section of this chemistry information sheet. Whole blood is not recommended for use as a sample.

SPECIMEN STORAGE AND STABILITY

1. Tubes of blood are to be kept closed at all times and in a vertical position. It is recommended that the serum or plasma be physically separated from contact with cells within two hours from the time of collection.[4]
2. Separated serum or plasma should not remain at room temperature longer than 8 hours. If assays are not completed within 8 hours, serum or plasma should be stored at +2°C to +8°C. If assays are not completed within 48 hours, or the separated sample is to be stored beyond 48 hours, samples should be frozen at -15°C to -20°C. Frozen samples should be thawed only once. Analyte deterioration may occur in samples that are repeatedly frozen and thawed.[4]
3. It is recommended that urine assays be performed within 2 hours of collection. For timed specimens, the collection container is to be kept in the refrigerator or on ice during the timed period. If a special preservative is required, it should be added to the container before urine collection begins.[5]

Additional specimen storage and stability conditions as designated by this laboratory:

SAMPLE VOLUME

A filled 0.5 mL sample cup is the optimum volume. For optimum primary sample tube volumes in primary tube samples and minimum volumes, refer to the Primary Tube Sample Template for your system.

CRITERIA FOR UNACCEPTABLE SPECIMENS

Refer to the PROCEDURAL NOTES section of this chemistry information sheet for information on unacceptable specimens.

Criteria for sample rejection as designated by this laboratory:

PATIENT PREPARATION

Special instructions for patient preparation as designated by this laboratory:

SPECIMEN HANDLING

Special instructions for specimen handling as designated by this laboratory:

REAGENTS

CONTENTS

Each kit contains the following items:

Two CR-E Reagent Cartridges (2 x 200 tests)

VOLUMES PER TEST

Sample Volume	
Serum/Plasma	10 µL
Urine	10 µL
Total Reagent Volume	240 µL
Cartridge Volumes	
A	180 µL
B	60 µL
C	– –

REACTIVE INGREDIENTS

REAGENT CONSTITUENTS

Creatine Amidinohydrolase (microbial)	8.64 kU/L
Sarcosine Oxidase (microbial)	2.88 kU/L
N-ethyl-N-(3-sulfopropyl)- 3-methylaniline	0.17 mmol/L
Creatinine amidohydrolase	32.4 kU/L
Peroxidase (vegetable)	0.48 kU/L
4-Aminoantipyrine	0.36 mmol/L
pH	7.5

Also non-reactive chemicals necessary for optimal system performance.

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

Reagent 2 (Compartment B) DANGER

H317	May cause an allergic skin reaction.
H334	May cause allergy or asthma symptoms or breathing difficulties if inhaled.
P261	Avoid breathing vapours.
P280	Wear protective gloves, protective clothing and eye/face protection.
P304+P340	IF INHALED: Remove person to fresh air and keep at rest in a position comfortable for breathing.
P333+P313	If skin irritation or rash occurs: Get medical advice/attention.
P342+P311	If experiencing respiratory symptoms: Call a POISON CENTER or doctor/physician.
P362+P364	Take off contaminated clothing and wash it before use.
	Peroxidase 1 - 10%

EUROPEAN HAZARD CLASSIFICATION

Reagent 2 (Compartment B) Xn;R42/43

R42/43	May cause sensitization by inhalation and skin contact.
S36/37	Wear suitable protective clothing and gloves.

MATERIALS NEEDED BUT NOT SUPPLIED WITH REAGENT KIT

SYNCHRON® Systems AQUA CAL 1 and 2
At least two levels of control material
Saline

DIL 1 for urine samples

REAGENT PREPARATION

No preparation is required.

ACCEPTABLE REAGENT PERFORMANCE

The acceptability of a reagent is determined by successful calibration and by ensuring that quality control results are within your facility's acceptance criteria.

REAGENT STORAGE AND STABILITY

CR-E reagent when stored unopened at +2°C to +8°C will obtain the shelf-life indicated on the cartridge label. Once opened, the reagent is stable for 30 days at +2°C to +8°C unless the expiration date is exceeded.

Reagent storage location:

CALIBRATION

CALIBRATOR REQUIRED

SYNCHRON® Systems AQUA CAL 1 and 2

CALIBRATOR PREPARATION

No preparation is required.

CALIBRATOR STORAGE AND STABILITY

1. If unopened, the calibrators should be stored at +2°C to +8°C until the expiration date printed on the calibrator bottle. Once opened, the calibrators are stable at room temperature for 30 days.
2. Repetitive refrigeration of the aqueous calibrators may facilitate crystal formation. Once removed from refrigerated storage, these calibrators should remain at room temperature.

Calibrator storage location:

CALIBRATION INFORMATION

1. The system must have a valid calibration factor in memory before control or patient samples can be run.
2. Under typical operating conditions the CR-E reagent cartridge must be calibrated every 14 days or with each new bottle of reagent and also with certain parts replacements or maintenance procedures, as defined in the UniCel DxC 600/800 System *Instructions For Use* (IFU) manual.
3. This assay has within-lot calibration available. For detailed calibration instructions, refer to the UniCel DxC 600/800 System *Instructions for Use* (IFU) manual.
4. The system will automatically perform checks on the calibration and produce data at the end of calibration. In the event of a failed calibration, the data will be printed with error codes and the system will alert the operator of the failure. For information on error codes, refer to the UniCel DxC 600/800 System *Instructions For Use* (IFU) manual.

TRACEABILITY

For Traceability information refer to the Calibrator instructions for use.

QUALITY CONTROL

At least two levels of control material should be analyzed daily. In addition, these controls should be run with each new calibration, with each new reagent cartridge, and after specific maintenance or troubleshooting procedures as detailed in the appropriate system manual. More frequent use of controls or the use of additional controls is left to the discretion of the user based on good laboratory practices or laboratory accreditation requirements and applicable laws.

The following controls should be prepared and used in accordance with the package inserts. Discrepant quality control results should be evaluated by your facility.

Table 1.0 Quality Control Material

CONTROL NAME	SAMPLE TYPE	STORAGE

TESTING PROCEDURE(S)

1. If necessary, prepare the reagent cartridge as described in the Reagent Preparation section of this chemistry information sheet and load the reagent onto the system.
2. After reagent load is completed, calibration may be required.
3. Program samples and controls for analysis.
4. After loading samples and controls onto the system, follow the protocols for system operations.

For detailed testing procedures, refer to the UniCel DxC 600/800 System *Instructions For Use* (IFU) manual.

CALCULATIONS

The system performs all calculations internally to produce the final reported result. The system will calculate the final result for sample dilutions made by the operator when the dilution factor is entered into the system during sample programming.

If calculation of creatinine clearance is desired, refer to References (3).

REPORTING RESULTS

REFERENCE INTERVALS

Each laboratory should establish its own reference intervals based upon its patient population. The reference intervals listed below were taken from literature.[6]

Table 2.0 Reference intervals

INTERVALS	SAMPLE TYPE	CONVENTIONAL UNITS	S.I. UNITS
Literature	Serum or Plasma (Male)	0.9 – 1.3 mg/dL	80 – 115 µmol/L
	Serum or Plasma (Female)	0.6 – 1.1 mg/dL	53 – 97 µmol/L
	Urine (Male)	800 – 2000 mg/24 hrs	7.1 – 17.7 mmol/24 hrs
	Urine (Female)	600 – 1800 mg/24 hrs	5.3 – 15.9 mmol/24 hrs
SYNCHRON	Serum or Plasma (Male)	0.61 – 1.24 mg/dL	54 – 110 µmol/L
	Serum or Plasma (Female)	0.44 – 1.00 mg/dL	39 – 89 µmol/L

INTERVALS	SAMPLE TYPE	CONVENTIONAL UNITS	S.I. UNITS
Laboratory			

Refer to References (7,8,9) for guidelines on establishing laboratory-specific reference intervals.

Additional reporting information as designated by this laboratory:

PROCEDURAL NOTES

ANTICOAGULANT TEST RESULTS

The following anticoagulants were assessed by Deming regression analysis with 53 paired human serum and plasma samples. Values of serum (X) ranging from 0.5 mg/dL to 25 mg/dL were compared with the values for plasma (Y) yielding the following results.

Table 3.0 Acceptable Anticoagulants

ANTICOAGULANT	LEVEL TESTED FOR IN VITRO INTERFERENCE	DEMING REGRESSION ANALYSIS
Lithium Heparin	14 Units/mL	Y = 0.997X - 0.005, r = 1.000
Sodium Heparin	14 Units/mL	Y= 1.001X - 0.003; r = 1.000

LIMITATIONS

If urine samples are cloudy or turbid, it is recommended that they be centrifuged prior transfer to sample cups.

INTERFERENCES

1. The following substances were tested for interference with this methodology:

Table 4.0 Interferences

SUBSTANCE	SOURCE	LEVEL TESTED	OBSERVED EFFECT ON ANALYTE
Acetoacetate	Acetoacetic acid lithium salt	500 mg/dL	NSI[a]
Lipemia	Intralipid[b]	500 mg/dL	NSI
Lipemia	Human	Serum Index 8	NSI
Ascorbic Acid	L-Ascorbic Acid	20 mg/dL	NSI
Glucose	D-Glucose	2000 mg/dL	NSI
Bilirubin (unconjugated)	Bovine	22.5 mg/dL	NSI
Bilirubin (Total)	Porcine	6.7 mg/dL DBIL	≤ - 0.4 mg/dL or 10%
		15.5 mg/dL TBIL	
Hemoglobin	RBC hemolysate	500 mg/dL	NSI
Dopamine	Dopamine Hydrochloride	15 µmol/L	NSI
N-Acetyl Cysteine[c]	SIGMA[d]	500 µg/mL	-6.3%

a NSI = No Significant Interference (within ±0.2 mg/dL or 6%).
b Registered trademarks are the property of their respective owners.
c Patients treated with N-Acetyl Cysteine (NAC) for an Acetaminophen overdose may generate a false low result for CR-E.
d SIGMA-Aldrich Co., St. Louis, MO.

2. Lipemic samples with visual turbidity >3+, or with a Lipemia Serum Index >8, should be ultracentrifuged and the analysis performed on the infranate.

Refer to References (10,11,12) for other interferences caused by drugs, disease and preanalytical variables.

PERFORMANCE CHARACTERISTICS

ANALYTIC RANGE

The SYNCHRON System(s) method for the determination of this analyte provides the following analytical ranges:

Table 5.0 Analytical Range

SAMPLE TYPE	CONVENTIONAL UNITS	S.I. UNITS
Serum or Plasma	0.1 – 25.0 mg/dL	9 – 2210 µmol/L
Urine	10 – 400 mg/dL	884 – 35360 µmol/L

Samples with concentrations exceeding the high end of the analytical range should be diluted with saline and reanalyzed.

REPORTABLE RANGE (AS DETERMINED ON SITE):

Table 6.0 Reportable Range

SAMPLE TYPE	CONVENTIONAL UNITS	S.I. UNITS

SENSITIVITY

Sensitivity is defined as the lowest measurable concentration which can be distinguished from zero with 95% confidence. Sensitivity for the CR-E determination is 0.1 mg/dL (9 µmol/L) for serum or plasma and 10 mg/dL (884 µmol/L) for urine.

EQUIVALENCY

Equivalency was assessed by Deming regression analysis of patient samples to accepted clinical methods.

Serum or plasma (in the range of 0.53 to 23.75 mg/dL):

Y (UniCel DxC Systems)	= 0.991X + 0.012
N	= 80
MEAN (UniCel DxC Systems CR-E Reagent)	= 3.05
MEAN (UniCel DxC Systems CR-S Reagent)	= 3.06
CORRELATION COEFFICIENT (r)	= 1.000

Urine in the range of 12.50 to 382.01 mg/dL:

Y (UniCel DxC Systems)	= 0.988X - 3.096
N	= 66
MEAN (UniCel DxC Systems CR-E Reagent)	= 153.5
MEAN (UniCel DxC Systems CR-S Reagent)	= 158.5
CORRELATION COEFFICIENT (r)	= 0.998

Refer to References (13) for guidelines on performing equivalency testing.

PRECISION

A properly operating SYNCHRON System(s) should exhibit precision values less than or equal to the following:

Table 7.0 Precision Values

TYPE OF PRECISION	SAMPLE TYPE	SD		CHANGEOVER VALUE[a]		% CV
		mg/dL	µmol/L	mg/dL	µmol/L	
Within-run	Serum/Plasma	0.10	8.8	3.30	291.7	3.0
	Urine	1.0	88	33	2917	3.0

Table 7.0 Precision Values, Continued

TYPE OF PRECISION	SAMPLE TYPE	SD		CHANGEOVER VALUE[a]		% CV
		mg/dL	µmol/L	mg/dL	µmol/L	
Total	Serum/Plasma	0.15	13.3	3.30	291.7	4.5
	Urine	1.5	133	33	2917	4.5

a When the mean of the test precision data is less than or equal to the changeover value, compare the test SD to the SD guideline given above to determine the acceptability of the precision testing. When the mean of the test precision data is greater than the changeover value, compare the test % CV to the guideline given above to determine acceptability. Changeover value = (SD guideline/CV guideline) x 100.

Comparative performance data for the UniCel DxC System evaluated using the CLSI/NCCLS Approved Guideline EP5-A2 appears in the table below.[14] Each laboratory should characterize their own instrument performance for comparison purposes.

Table 8.0 CLSI/NCCLS EP5-A2 Precision Estimate Method

TYPE OF IMPRECISION	SAMPLE TYPE	No. Systems	No. Data Points[a]	Test Mean Value (mg/dL)	CLSI/NCCLS EP5-A2 Precision Estimate Method	
					SD	% CV
Within-run	Serum	Control 1	80	0.64	0.01	2.1
	Serum	Control 2	80	4.09	0.01	0.3
	Serum	Control 3	80	7.56	0.03	0.3
	Serum	Human Pool	80	1.50	0.01	0.7
	Urine	Control 1	80	66.45	0.31	0.5
	Urine	Control 2	80	146.61	0.60	0.4
Total	Serum	Control 1	80	0.64	0.02	2.5
	Serum	Control 2	80	4.09	0.03	0.7
	Serum	Control 3	80	7.56	0.06	0.8
	Serum	Human Pool	80	1.50	0.01	0.9
	Urine	Control 1	80	66.45	0.68	1.0
	Urine	Control 2	80	146.61	1.47	1.0

a The point estimate is based on the pooled data from one system, run for twenty days, two runs per day, two observations per run on an instrument operated and maintained according to the manufacturer's instructions.

Refer to References (14) for guidelines on performing precision testing.

NOTICE

These degrees of precision and equivalency were obtained in typical testing procedures on UniCel DxC System(s) and are not intended to represent the performance specifications for this reagent.

ADDITIONAL INFORMATION

For more detailed information on UniCel DxC Systems, refer to the appropriate system manual.

SHIPPING DAMAGE

If damaged product is received, notify your Beckman Coulter Clinical Support Center.

REVISION HISTORY

Revision AB

Revised Methodology, Analytic Range, and Sensitivity sections.

Revision AC

Updated corporate address; updated European Hazard Classification.

Revision AD

Added Revision History.

Revision AE

Revised Interferences section.

Revision AF

Added new language requirement: Czech, and Korean.

Revision AG

Removed references to CX and LX systems as they are discontinued effective 12/2013.

Added Beckman Coulter trademark statement and disclaimer.

Revision AH

Added GHS Classification information

Revision AJ

Added N- Acetyl Cysteine substance information in interference table.

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