BECKMAN COULTER

SYNCHRON System(s)
Chemistry Information Sheet

CR-S
Creatinine

REF A40920

For *In Vitro* Diagnostic Use

Rx Only

ANNUAL REVIEW

Reviewed by	Date	Reviewed by	Date

PRINCIPLE

INTENDED USE

CR-S reagent, when used in conjunction with UniCel DxC 600/800 System(s) and SYNCHRON Systems AQUA CAL 1 and 2, is intended for the quantitative determination of creatinine concentration in human serum, plasma or urine.

CLINICAL SIGNIFICANCE

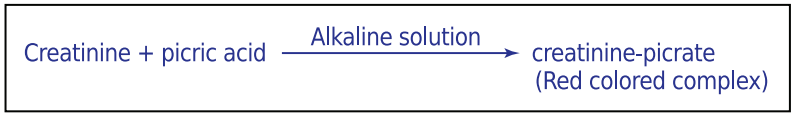
Creatinine measurements are used in the diagnosis and treatment of renal diseases, in monitoring renal dialysis, and as a calculation basis for measuring other urine analytes.

METHODOLOGY

CR-S reagent is used to measure the creatinine concentration by a modified rate Jaffé method.[1,2,3] In the reaction, creatinine combines with picrate in an alkaline solution to form a creatinine-picrate complex.

The SYNCHRON System(s) automatically proportions the appropriate sample and reagent volumes into the cuvette. The ratio used is one part sample to 11 parts reagent for serum and one part sample to 73 parts reagent for urine. The System monitors the change in absorbance at 520 nanometers. This change in absorbance is directly proportional to the concentration of CR-S in the sample and is used by the System to calculate and express CR-S 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.[4] Freshly drawn serum or 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.[5]
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.[5]
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.[6]

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-S Reagent Cartridges (2 x 300 tests)

VOLUMES PER TEST

Sample Volume	
Serum/Plasma	20 µL
Urine	3 µL
Total Reagent Volume	219 µL
Cartridge Volumes	
A	175 µL
B	44 µL
C	– –

REACTIVE INGREDIENTS

REAGENT CONSTITUENTS

Picric Acid	8.1 mmol/L
Buffered to pH	> 13.3

Also non-reactive chemicals necessary for optimal system performance.

GHS HAZARD CLASSIFICATION

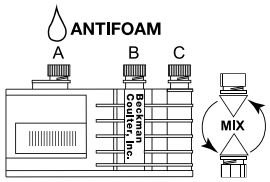
Creatinine Reagent (Compartment A)	DANGER	
		
		
		
	H300	Fatal if swallowed.
	H311	Toxic in contact with skin.
	H314	Causes severe skin burns and eye damage.
	H360	May damage fertility or the unborn child.
	P201	Obtain special instructions before use.
	P280	Wear protective gloves, protective clothing and eye/face protection.
	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.
		Boric Acid < 5%
		Tetramethylammonium Hydroxide 10 - 20%
		Diethanolamine Dodecylsulfate 1 - 5%
Creatinine Reagent (Compartment B)	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.
	P304+P340	IF INHALED: Remove person to fresh air and keep at rest in a position comfortable for breathing.
	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 <1%

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

MATERIALS NEEDED BUT NOT SUPPLIED WITH REAGENT KIT

SYNCHRON Systems AQUA CAL 1 and 2
Antifoam P/N 445967
At least two levels of control material
Saline

REAGENT PREPARATION



1. Add 1 drop of Antifoam to reagent compartment A. Do not use more than the recommended volume of Antifoam.
2. Replace cartridge caps and gently invert the cartridge several times to ensure adequate mixing.

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-S reagent, when stored unopened at room temperature, will obtain the shelf-life indicated on the cartridge label. Once opened, the reagent is stable for 15 days at +2°C to +8°C unless the expiration date is exceeded. DO NOT FREEZE.

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 creatinine assay must be calibrated every 5 days or with each new cartridge 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 Systems *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 print out with error codes and the system will alert the operator of the failure. An explanation of these error codes can be found in the UniCel DxC 600/800 Systems *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 Systems *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 (4).

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.[7]

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 – 1.0 mg/dL	39 – 89 µmol/L

INTERVALS	SAMPLE TYPE	CONVENTIONAL UNITS	S.I. UNITS
Laboratory			

Refer to References (8,9,10) for guidelines on establishing laboratory-specific reference intervals.

Additional reporting information as designated by this laboratory:

PROCEDURAL NOTES

ANTICOAGULANT TEST RESULTS

If plasma is the sample of choice, the following anticoagulants were found to be compatible with this method based on a study of 20 healthy volunteers:

Table 3.0 Acceptable Anticoagulants

ANTICOAGULANT	LEVEL TESTED FOR IN VITRO INTERFERENCE	DEMING REGRESSION ANALYSIS
Lithium Heparin	14 Units/mL	Y= 0.985X + 0.02; r = 0.999
Sodium Heparin	14 Units/mL	Y= 1.006X - 0.02; r = 0.999

LIMITATIONS

1. If urine samples are cloudy or turbid, it is recommended that they be centrifuged prior transfer to sample cups.
2. Sample discoloration can interfere with photometric tests. The users of these test systems should evaluate the sample quality and identify potentially interfering substances in these samples. This evaluation is normally done by visual assessment.[11]

INTERFERENCES

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

Table 4.0 Interferences

SUBSTANCE	SOURCE	LEVEL TESTED	OBSERVED EFFECT[a]
Bilirubin	Porcine	15.0 mg/dL	NSI[b]
		22.5 mg/dL	-0.5 mg/dL
Lipemia	Human	+4 (visual)	NSI
Hemoglobin	Human	500 mg/dL	NSI
Acetoacetate	Acetoacetic acid lithium salt	20 mg/dL	NSI
Pyruvate	Pyruvic acid	10 mg/dL	NSI
Methyl dopa	Methyl dopa HCl	5 mg/dL	NSI
Gentisic Acid	2,5-dihydroxybenzoic acid	50 mg/dL	NSI
Cephalothin	7-[2-thienylacetamido]-cephalosporanic acid sodium salt	100 mg/dL	NSI
Cefotaxime	Sodium Salt	50 mg/dL	NSI
Cefoxitin	Sodium Salt	12.5 mg/dL	NSI
		25.0 mg/dL	+0.7 mg/dL
Cephalosporin	Zinc salt	10 mg/dL	NSI

a Plus (+) or minus (-) signs in this column signify positive or negative interference.
b NSI = No Significant Interference (within ±0.4 mg/dL or 4%).

Refer to References (12,13,14,15) 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	0.3 – 25.0 mg/dL	27 – 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

EQUIVALENCY

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

Serum or Plasma (in the range of 0.3 to 25.0 mg/dL):

Y (UniCel DxC Systems)	= 0.962X + 0.03
N	= 105
MEAN (UniCel DxC Systems)	= 3.8
MEAN (SYNCHRON CX Systems)	= 3.9
CORRELATION COEFFICIENT (r)	= 1.000

Urine (in the range of 17.1 to 391.5 mg/dL):

Y (UniCel DxC Systems)	= 1.002X + 3.67
N	= 75
MEAN (UniCel DxC Systems)	= 141.4
MEAN (SYNCHRON CX Systems)	= 137.4
CORRELATION COEFFICIENT (r)	= 0.999

Serum (in the range of 0.34 to 22.45 mg/dL):

Y (UniCel DxC Systems)	= 1.02X -0.08
N	= 39
MEAN (UniCel DxC Systems)	= 4.40
MEAN (Isotope Dilution Mass Spectroscopy reference procedure (16))	= 4.41
CORRELATION COEFFICIENT (r)	= 0.9997

Refer to References (17) 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	0.2	18	10.0	900	2.0
	Urine	2.0	177	100	8850	2.0
Total	Serum/Plasma	0.3	27	10.0	900	3.0
	Urine	3.0	266	100	8866	3.0

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(s) evaluated using the NCCLS Proposed Guideline EP5-A appears in the table below.[18] Each laboratory should characterize their own instrument performance for comparison purposes.

Table 8.0 NCCLS EP5-A Precision Estimate Method

TYPE OF IMPRECISION	SAMPLE TYPE	No. Systems	No. Data Points[a]	Test Mean Value (mg/dL)	EP5-A Calculated Point Estimates	
					SD	% CV
Within-run	Serum	Level 1	80	0.6	0.05	9.4
	Serum	Level 2	80	7.2	0.06	0.9
	Urine	Level 1	80	90.1	1.21	1.4
	Urine	Level 2	80	244.0	3.67	1.5
Total	Serum	Level 1	80	0.6	0.05	9.5
	Serum	Level 2	80	7.2	0.12	1.7
	Urine	Level 1	80	90.1	1.70	1.9
	Urine	Level 2	80	244.0	4.22	1.7

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 (18) 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 System(s), refer to the appropriate system manual.

SHIPPING DAMAGE

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

REVISION HISTORY

Revision AE

Updated corporate address; updated European Hazard Classification and removed EDTA as an Acceptable Anticoagulant claim.

Revision AF

Revised Materials Needed section.

Revision AG

Added Reagent Preparation visual aid to the Reagent Preparation section.

Revision AH

Added Revision History

Revision AJ

Added new language requirement: Czech, and Korean.

Revision AK

Added GHS Classification information

Revision AL

Added new language requirement: Romanian

Revision AM

Added limitation statement and reference.

Revision AN

Updates to comply with requirements per Beckman Coulter Global Labeling Policy.

Revision AP

Additional changes to comply with requirements per Beckman Coulter Global Labeling Policy.

Revision AR

Added new language requirement: Bulgarian, Serbian, and Vietnamese. Additional changes to comply with requirements per Beckman Coulter Global Labeling Policy.

SYMBOLS KEY

Table 9.0

REF	Catalogue Number	IVD	In Vitro Diagnostic
CONTENTS	Contents		Temperature limit
	Manufacturer		Expiration Date
LOT	Batch code	SDS	Safety Data Sheet
CE	CE Mark		Consult Instructions for Use
EC REP	Authorized Representative in the European Community		Date of Manufacture
	Do Not Freeze	DANGER	DANGER
	Do not reuse		
Made in USA of US and Foreign Components		Made in USA of US and Foreign Components	

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