

SYNCHRON CX[®] System(s) Chemistry Information Sheet

CR-S
Creatinine
Kit Reorder # A40920

For In Vitro Diagnostic Use

ANNUAL REVIEW

Reviewed by:	Date	Reviewed by:	Date
Refer to "Review and Revision Coversheet" in front of each method.			

PRINCIPLE

INTENDED USE

CR-S reagent, when used in conjunction with SYNCHRON CX[®] System(s) and Synchron CX[®] Calibrator Level 1 and 2, is intended for the quantitative determination of Creatinine (CR-S) concentration in human serum, plasma or urine.

The creatinine method is calibrated to be traceable to an isotope dilution mass spectrometry (IDMS) reference method. The creatinine value will be used to automatically calculate and report an estimated GFR (eGFR) in adults using the IDMS-traceable MDRD (Modification of Diet in Renal Disease) Study equation as recommended by NKDEP (National Kidney Disease Education Program).

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.

An estimated GFR (eGFR) from serum creatinine is a practical way to identify people with chronic kidney disease (CKD) who might otherwise go untreated, and to monitor those with risk factors for CKD, i.e., diabetes, hypertension, cardiovascular disease, or family history of kidney disease.

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 CX[®] 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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eGFR CALCULATION using the IDMS-Traceable MDRD Equation

$$\text{eGFR}(\text{mL}/\text{min}/1.73 \text{ m}^2) = 175 \times (\text{S}_{\text{cr}})^{-1.154} \times (\text{Age})^{-0.203} \times (0.742 \text{ if female}) \times (1.210 \text{ if African American})$$

The equation requires four variables:

1. Serum, or plasma, creatinine (S_{cr})
2. Age in years (18 years or older)
3. Sex
4. Race (African American or not)

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:

Refer to “Sample Integrity in Chemistry” write up in “CX5 Procedures Manual

SAMPLE VOLUME

A filled 0.5 mL sample cup is the optimum volume. For optimum volume in primary tube samples, refer to Primary Sample Tube Chart Template (P/N 248511) for minimum volume requirements.

CRITERIA FOR UNACCEPTABLE SPECIMENS

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

CRITERIA FOR SAMPLE REJECTION AS DESIGNATED BY THIS LABORATORY:

Refer to “**Sample Integrity in Chemistry**” write up in “**CX5 Procedures Manual**”

PATIENT PREPARATION

SPECIAL INSTRUCTIONS FOR PATIENT PREPARATION AS DESIGNATED BY THIS LABORATORY:

Refer to “**Sample Integrity in Chemistry**” write up in “**CX5 Procedures Manual**”

SPECIMEN HANDLING

SPECIAL INSTRUCTIONS FOR SPECIMEN HANDLING AS DESIGNATED BY THIS LABORATORY:

Refer to “**Sample Integrity in Chemistry**” write up in “**CX5 Procedure Manual**”

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.

EUROPEAN HAZARD CLASSIFICATION

Creatinine Reagent (Compartment A)	T+;R27	Very toxic in contact with skin.
	R34	Causes burns.
	S26	In case of contact with eyes, rinse immediately with plenty of water and seek medical advice.
	S27	Take off immediately all contaminated clothing.
	S36/37/39	Wear suitable protective clothing, gloves and eye/face protection.
	S9	Keep container in a well-ventilated place.

MATERIALS NEEDED BUT NOT SUPPLIED WITH REAGENT KIT

Synchron CX[®] Calibrator Level 1 and 2

Antifoam

At least two levels of control material

Saline

REAGENT PREPARATION

Add 1 drop of Antifoam to reagent compartment A. Mix gently. Do not use more than the recommended volume of Antifoam.

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, as defined in the CONTROL PROCEDURES section of this manual.

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 20 days at +2°C to +8°C unless the expiration date is exceeded. DO NOT FREEZE.

REAGENT STORAGE LOCATION:

Chemistry – room temperature

CALIBRATION

CALIBRATOR REQUIRED

Synchron CX[®] Calibrator Level 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:

Refer to “**Calibrators Quick Reference**” chart in “**CX5 Procedure Manual**”

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-S assay must be calibrated every 7 days or with each new cartridge of reagent, and also with certain parts replacements or maintenance procedures, as defined in the SYNCHRON CX *Operating Instructions* manual. This assay has within lot calibration available. Refer to section 6 of the SYNCHRON CX *Operating Instructions* manual for information on this feature.
3. For detailed calibration instructions refer to Section 6 of the SYNCHRON CX *Operating Instructions* 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. The explanation of these error codes can be found in Appendix G of Section 10 in the SYNCHRON CX *Operating Instructions* 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 *SYNCHRON CX Operating Instructions* manual. More frequent use of controls or the use of additional controls is left to the discretion of the user based on work load and work flow.

The following controls should be prepared and used in accordance with the package inserts. Copies of these inserts can be found in the CONTROL PROCEDURES section of this manual. Discrepant quality control results should be evaluated and handled as described in the CONTROL PROCEDURES section of this manual.

TABLE 1 QUALITY CONTROL MATERIAL

CONTROL NAME	SAMPLE TYPE	STORAGE
Refer to “ CX5 Delta Control Analysis ” in “ CX5 Procedure Manual ” for control material used and storage conditions. Control preparation and acceptance of QC results are in “ CX5 Procedures Manual ”		

TESTING PROCEDURE(S)

1. If necessary prepare reagent cartridge as defined in the Reagent Preparation section of this chemistry information sheet and load the reagent onto the system as directed in Section 6 of the *SYNCHRON CX Operating Instructions* manual.
2. After reagent load is completed, calibration may be required. Refer to Section 6 of the *SYNCHRON CX Operating Instructions* manual for details of the calibration procedure.
3. Program samples and controls for analysis as directed in Section 6 of the *SYNCHRON CX Operating Instructions* manual.
4. After loading samples and controls onto the system, follow the protocols for system operation as directed in Section 6 of the *SYNCHRON CX Operating Instructions* manual.

CALCULATIONS

The system performs all calculations internally to produce the final reported result. *SYNCHRON CX4/5* Systems do not calculate the final result for sample dilutions made by the operator. In these cases, the result produced by the instrument must be multiplied by the dilution factor before reporting the final result. *SYNCHRON CX4CE/5CE/7* Systems (including the *CX DELTA* and *CX PRO* Systems) 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 REFERENCE INTERVALS

Table 2. 0 Creatinine Reference Intervals

INTERVAL	SAMPLE TYPE	CONVENTIONAL UNITS	S.I. UNITS
Literature ⁸ (NOT IDMS)	Serum or Plasma (Male)	0.9 to 1.3 mg/dL	80 to 115 umol/L
	Serum or Plasma (Female)	0.6 to 1.1mg/dL	53 to 97 umol/L
	Urine (Male)	800 to 2000 mg/24 hrs	7.1 to 17.7 mmol/24 hrs
	Urine (Female)	600 to 1800 mg/24 hrs	5.3 to 15.9 mmol/24 hrs
SYNCHRON (NOT IDMS)	Serum or Plasma (Male)	0.7 to 1.2 mg/dL	52 to 106 umol/L
	Serum or Plasma (Female)	0.4 to 1.0 mg/dL	35 to 88 umol/L

INTERVAL	SAMPLE TYPE	CONVENTIONAL UNITS		S.I. UNITS
Laboratory	Serum or Plasma	0 – 1 yr:	0.30 – 0.70 mg/dL	To convert to umol/L, multiply by 88.4
		1 – 18 yrs:	0.30 – 0.90 mg/dL	
		Male** ≥19 yrs:	0.64 -1.20 mg/dL	
		Female** ≥19 yrs:	0.42 –1.06 mg/dL	
		**IDMS traceable		

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

Estimated GFR(eGFR) Reference Range: >60 mL/min for adults ≥18 years.

Procedures for reporting results to the appropriate personnel can be found in the HOW TO REPORT RESULTS section of this manual.

ADDITIONAL REPORTING INFORMATION AS DESIGNATED BY THIS LABORATORY:

Refer to “CX5 Linearity and Reportable Range” chart in “CX5 Procedures Manual”

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 ACCEPTABLE ANTICOAGULANTS

ANTICOAGULANT	LEVEL TESTED FOR IN VITRO INTERFERENCE	AVERAGE PLASMA-SERUM BIAS
Ammonium Heparin	29 Units/mL	NSI ^a
EDTA	3.0 mg/mL	NSI
Lithium Heparin	29 Units/mL	NSI
Potassium Oxalate/Sodium Fluoride	4.0 / 5.0 mg/mL	NSI
Sodium Citrate	6.0 mg/mL	NSI
Sodium Heparin	29 Units/mL	NSI

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 INTERFERENCES

SUBSTANCE	SOURCE	CONCENTRATION	OBSERVED EFFECT ON ANALYTE ^b
Acetoacetate	Acetoacetic acid lithium salt	20 mg/dL	+ 0.5 mg/dL
Pyruvate	Pyruvic acid	0.9 mg/dL	+ 1.8 mg/dL
		2.0 mg/dL	+ 6.0 mg/dL
Methyl dopa	Methyl dopa HCl	2.5 mg/dL	+ 0.8 mg/dL
Gentisic Acid	2,5-dihydroxybenzoic acid	50 mg/dL	- 0.7 mg/dL
Cephalothin	7-[2-thienylacetamido]-cephalosporanic acid sodium salt	10 mg/dL	+ 0.2 mg/dL
		100 mg/dL	+ 1.6 mg/dL
Cefotaxime	Cefotaxime sodium salt	90 mg/dL	+ 0.1 mg/dL
Cefoxitin	Cefoxitin sodium salt	120 µg/mL	0.0 mg/dL
Cephalosporin	Zinc salt	40 µg/mL	0.0 mg/dL
Bilirubin	Bilirubin (unconjugated)	10 mg/dL	- 0.3 mg/dL
Hemoglobin	RBC hemolysate	750 mg/dL	≤ 0.2 mg/dL

2. Lipemic samples >3+ should be ultra-centrifuged and the analysis performed on the infranate.
3. Refer to References (11,12,13) for other interferences caused by drugs, disease and preanalytical variables.

PERFORMANCE CHARACTERISTICS

Analytic Range

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

TABLE 5 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 REPORTABLE RANGE

SAMPLE TYPE	CONVENTIONAL UNITS	S.I. UNITS
Refer to “CX5 Linearity and Reportable Range” chart in “CX5 Procedures Manual”		

EQUIVALENCY

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

Serum or plasma:

Y (SYNCHRON CX Systems) ^c	= 0.989X + 0.03
N	= 105
MEAN (SYNCHRON CX Systems) ^c	= 4.26
MEAN (SYNCHRON AS [®])	= 4.28
CORRELATION COEFFICIENT (r)	= 0.9987

Urine:

Y (SYNCHRON CX Systems) ^d	= 1.042X + 0.16
N	= 42
MEAN (SYNCHRON CX Systems) ^d	= 90.1
MEAN (SYNCHRON AS [®])	= 86.2
CORRELATION COEFFICIENT (r)	= 0.9995

Serum:

Y (SYNCHRON CX Systems) ^e	= 0.99 X + - 0.04
N	= 39
MEAN (SYNCHRON CX Systems) ^e	= 4.35

Serum:

MEAN (Isotope Dilution Mass Spectroscopy reference procedure (14)) = 4.40

CORRELATION COEFFICIENT (r) = 0.9994

Refer to References (15) for guidelines on performing equivalency testing.

PRECISION

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

TABLE 7 PRECISION VALUES

TYPE OF PRECISION	SAMPLE TYPE	1 SD		CHANGEOVER VALUE ^f		% CV
		mg/dL	μmol/L	mg/dL	μmol/L	
Within-run	Serum/Plasma	0.2	18	6.7	600	3.0
	Urine	2.0	177	66.7	5,900	3.0
Total	Serum/Plasma	0.3	27	6.7	600	4.5
	Urine	3.0	266	66.7	5,900	4.5

Refer to References (16) for guidelines on performing precision testing.

NOTICE

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

ADDITIONAL INFORMATION

For more detailed information on SYNCHRON CX Systems, refer to the appropriate SYNCHRON CX manual.

SHIPPING DAMAGE

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

REFERENCES

1. Jaffe, M. Z., *Physiol. Chem.*, 10:391 (1886).
2. Vasiliades, J., *Clin. Chem. Acta*, 22:1664 (1976).
3. Heinegard, D., Tiderstrom, G., *Clin. Chem. Acta*, 43:305 310 (1973).
4. Tietz, N. W., "Specimen Collection and Processing; Sources of Biological Variation", *Textbook of Clinical Chemistry*, 2nd Edition, W. B. Saunders, Philadelphia, PA (1994).
5. National Committee for Clinical Laboratory Standards, *Procedures for the Handling and Processing of Blood Specimens*, Approved Guideline, NCCLS publication H18-A, Villanova, PA (1990).
6. National Committee for Clinical Laboratory Standards, *Routine Urinalysis and Collection, Transportation and Preservation of Urine Specimens*, Tentative Guideline, NCCLS publication GP16-T, Villanova, PA (1992).
7. Tietz, N. W., *Clinical Guide to Laboratory Tests*, 2nd Edition, W. B. Saunders, Philadelphia, PA (1990).
8. National Committee for Clinical Laboratory Standards, *How to Define, Determine, and Utilize Reference Intervals in the Clinical Laboratory*, Approved Guideline, NCCLS publication C28-A, Villanova, PA (1994).
9. Tietz, N. W., ed., *Fundamentals of Clinical Chemistry*, 3rd Edition, W. B. Saunders, Philadelphia, PA (1987).
10. Henry, J. B., *Clinical Diagnosis and Management by Laboratory Methods*, 18th Edition, W. B. Saunders Company, Philadelphia, PA (1991).
11. Young, D. S., *Effects of Drugs on Clinical Laboratory Tests*, 3rd Edition, AACC Press, Washington, D.C. (1990).
12. Friedman, R. B., Young, D. S., *Effects of Disease on Clinical Laboratory Tests*, 2nd Edition, AACC Press, Washington, D.C. (1989).
13. Young, D. S., *Effects of Preanalytical Variables on Clinical Laboratory Tests*, AACC Press, Washington, D.C. (1993).
14. Stöckl D, Reinauer H., *Clin Chem* 39:993-1000 (1993).
15. National Committee for Clinical Laboratory Standards, *Method Comparison and Bias Estimation Using Patient Samples*, Tentative Guideline, NCCLS publication EP9-T, Villanova, PA (1993).

16. National Committee for Clinical Laboratory Standards, *Precision Performance of Clinical Chemistry Devices*, Tentative Guideline, 2nd Edition, NCCLS publication EP5-T2, Villanova, PA (1992).
17. [National Kidney Disease Education Program, *Suggestions for Laboratories*, \(February 2007\).](#)



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ENDNOTES

- a NSI = No Significant Interference (within ± 0.4 mg/dL or 6%).
- b Plus (+) or minus (-) signs in this column signify positive or negative interference.
- c Data shown was collected using the SYNCHRON CX4/CX5 Systems. Equivalency between SYNCHRON CX Systems has been established by Deming regression analysis to SYNCHRON CX4/CX5 Systems.
- d Data shown was collected using the SYNCHRON CX4/CX5 Systems. Equivalency between SYNCHRON CX Systems has been established by Deming regression analysis to SYNCHRON CX4/CX5 Systems.
- e Data shown was collected using the SYNCHRON CX4/CX5 Systems. Equivalency between SYNCHRON CX Systems has been established by Deming regression analysis to SYNCHRON CX4/CX5 Systems.
- f 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.