

**SYNCHRON® System(s)
Chemistry Information Sheet**

**CRP
C-Reactive Protein
REF (200 tests/cartridge) 465131**

For In Vitro Diagnostic Use

ANNUAL REVIEW

Reviewed by:	Date	Reviewed by:	Date

PRINCIPLE

INTENDED USE

CRP reagent, when used in conjunction with SYNCHRON LX® System(s), UniCel® DxC 600/800 System(s) and SYNCHRON® Systems CAL 5 Plus, is intended for quantitative determination of c-reactive protein concentration in human serum or plasma.

CLINICAL SIGNIFICANCE

C-reactive protein measurements are useful in the clinical evaluation of stress, trauma, infection, inflammation, and surgery.

METHODOLOGY

CRP reagent is used to measure the c-reactive protein concentration by a turbidimetric method.^{1,2} In the reaction, c-reactive protein combines with specific antibody to form insoluble antigen-antibody complexes.

The SYNCHRON® System(s) automatically proportions the appropriate sample and reagent volumes into a cuvette. The ratio used is one part sample to 26 parts reagent. The system monitors the change in absorbance at 340 nanometers. This change in absorbance is proportional to the concentration of C-reactive protein in the sample and is used by the System to calculate and express C-reactive protein concentration based upon a single-point adjusted, pre-determined calibration curve.

CHEMICAL REACTION SCHEME



E015217LEPS

SPECIMEN

TYPE OF SPECIMEN

Biological fluid samples should be collected in the same manner routinely used for any laboratory test.³ Freshly drawn serum or plasma are the preferred specimens. Acceptable anticoagulants are listed in the PROCEDURAL NOTES section of this chemistry information sheet. Whole blood or urine are not recommended for use as a sample.

SPECIMEN STORAGE AND STABILITY

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

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

ADDITIONAL SPECIMEN STORAGE AND STABILITY CONDITIONS AS DESIGNATED BY THIS LABORATORY:

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SAMPLE VOLUME

The optimum volume, when using a 0.5 mL sample cup, is 0.3 mL of sample. For optimum primary sample tube volumes 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:

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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 CRP Reagent Cartridges (2 x 200 tests)

One lot-specific Parameter Card

VOLUMES PER TEST

Sample Volume	10 µL
ORDAC Sample Volume	4 µL
Total Reagent Volume	260 µL
Cartridge Volumes	
A	250 µL
B	--
C	10 µL

REACTIVE INGREDIENTS

REAGENT CONSTITUENTS

Polyclonal anti-CRP Antibody (Goat)	3.5 mL
Reaction Buffer	63.4 mL

Also non-reactive chemicals necessary for optimal system performance.



CAUTION

Sodium azide preservative may form explosive compounds in metal drain lines. See National Institute for Occupational Safety and Health Bulletin: Explosive Azide Hazards (8/16/76).

MATERIALS NEEDED BUT NOT SUPPLIED WITH REAGENT KIT

SYNCHRON[®] Systems CAL 5 Plus
At least two levels of control material
Saline

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

CRP 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 60 days at +2°C to +8°C unless the expiration date is exceeded. DO NOT FREEZE.

REAGENT STORAGE LOCATION:

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CALIBRATION

CALIBRATOR REQUIRED

SYNCHRON[®] Systems CAL 5 Plus

CALIBRATOR PREPARATION

No preparation is required.

CALIBRATOR STORAGE AND STABILITY

SYNCHRON[®] Systems CAL 5 Plus is stable until the expiration date printed on the calibrator bottle if stored capped in the original container at +2°C to +8°C.

 CAUTION

Because this product is of human origin, it should be handled as though capable of transmitting infectious diseases. Each serum or plasma donor unit used in the preparation of this material was tested by United States Food and Drug Administration (FDA) approved methods and found to be negative for antibodies to HIV and HCV and nonreactive for HbsAg. Because no test method can offer complete assurance that HIV, hepatitis B virus, and hepatitis C virus or other infectious agents are absent, this material should be handled as though capable of transmitting infectious diseases. This product may also contain other human source material for which there is no approved test. The FDA recommends such samples to be handled as specified in Centers for Disease Control's Biosafety Level 2 guidelines.⁵

CALIBRATOR STORAGE LOCATION:

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CALIBRATION INFORMATION

1. The system must have a lot-specific parameter card and a valid calibration adjustment in memory before controls or patient samples can be run.
2. Under typical operating conditions the CRP reagent cartridge must be calibrated every 30 days and also with certain parts replacements or maintenance procedures, as defined in the SYNCHRON LX *Maintenance Manual and Instrument Log*, or the UniCel DxC 600/800 System *Instructions For Use* (IFU) manual. This assay has within-lot calibration available. Refer to the SYNCHRON LX *Operations Manual*, or the UniCel DxC 600/800 System *Instructions For Use* (IFU) manual for information on this feature.
3. For detailed calibration instructions, refer to the SYNCHRON LX *Operations Manual*, or 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 SYNCHRON LX *Diagnostics and Troubleshooting Manual*, or 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 QUALITY CONTROL MATERIAL

CONTROL NAME	SAMPLE TYPE	STORAGE

TESTING PROCEDURE(S)

1. If necessary, 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 *SYNCHRON LX Operations Manual*, or the *UniCel DxH 600/800 System Instructions For Use (IFU)* manual.

CALCULATIONS

The SYNCHRON® System(s) 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.

REPORTING RESULTS

Equivalency between the SYNCHRON LX and UniCel DxH 600/800 Systems has been established. Chemistry results between these systems are in agreement and data from representative systems may be shown.

REFERENCE INTERVALS

Each laboratory should establish its own reference intervals based upon its patient population. The following reference intervals were taken from literature and a study performed on SYNCHRON Systems.⁶

TABLE 2 REFERENCE INTERVALS

INTERVALS	SAMPLE TYPE	CONVENTIONAL UNITS	S.I. UNITS
Literature	Serum or Plasma	< 1.0 mg/dL	< 10.0 mg/L
SYNCHRON	Serum or Plasma	< 1.0 mg/dL	< 10.0 mg/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:

REMARKS: OTHER INFORMATION IS DESIGNATED BY THIS CHECKBOX:

PROCEDURAL NOTES

ANTICOAGULANT TEST RESULTS

The following anticoagulants were assessed by Deming regression analysis with 50 paired human serum and plasma samples. Values of serum (X) ranging from 0.7 mg/dL to 14.9 mg/dL were compared with the values for plasma (Y) yielding the following results.

Table 3 Anticoagulant Test Results^a

ANTICOAGULANT	LEVEL OF ANTICOAGULANT TESTED	DEMING REGRESSION ANALYSIS (mg/dL)
Lithium Heparin	14 Units/mL	$Y = 1.042X - 0.45$; $r = 0.977$
Sodium Heparin	14 Units/mL	$Y = 0.994X - 0.07$; $r = 0.989$

LIMITATIONS

Neonatal samples should not be tested using the SYNCHRON CRP turbidimetric assay.^{10, 11}

INTERFERENCES

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

Table 4 Interferences^b

SUBSTANCE	SOURCE	LEVEL TESTED	OBSERVED EFFECT
Hemoglobin	RBC hemolysate	500 mg/dL	NSI ^c
Bilirubin	Porcine	30 mg/dL	NSI
Lipemia	Human	1+	NSI
Rheumatoid Factor	Human	400 IU/mL	NSI

2. Lipemic specimens should be delipidated by ultra centrifugation (90,000 x g for 10 minutes) prior to determination of CRP concentration.
3. Refer to References (12,13,14) for other interferences caused by drugs, disease and preanalytical variables.

PERFORMANCE CHARACTERISTICS

Analytic Range

The SYNCHRON® System(s) method for the determination of c-reactive protein provides the following analytical range:

TABLE 5 ANALYTICAL RANGE

SAMPLE TYPE	CONVENTIONAL UNITS	S.I. UNITS
Serum or Plasma	0.5 – 20.0 mg/dL	5.0 – 200.0 mg/L
Serum or Plasma (ORDAC)	15.0 – 48.8 mg/dL	150.0 – 488.0 mg/L

Samples with concentrations outside of the analytical range will be reported as "<0.5 mg/dL" ("<5.0 mg/L") or ">20 mg/dL" (">200.0 mg/L"). (ORDAC "<15.0 mg/dL" or ">48.8 mg/dL")

Samples reported out as greater than the analytical range should be confirmed by enabling ORDAC, or diluting with saline, and reanalyzing. If manual dilution is used the appropriate dilution factor should be applied to the reported result.

Samples reported out as "SUPPRESSED" due to RXN ERROR should be reanalyzed.

REPORTABLE RANGE (as determined on site):

TABLE 6 REPORTABLE RANGE

SAMPLE TYPE	CONVENTIONAL UNITS	S.I. UNITS

Samples flagged as "**Results Suppressed, Blank Rate-High**" should NOT be diluted and re-assayed. It is recommended an alternate method be used.

SENSITIVITY

Sensitivity is defined as the lowest measurable concentration which can be distinguished from zero with 95% confidence. Sensitivity for CRP determination is 0.5 mg/dL (5.0 mg/L).

EQUIVALENCY

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

Serum or plasma (in the range of 0.6 to 15.0 mg/dL):

Y (SYNCHRON LX Systems)	= 0.982X - 0.04
N	= 77
MEAN (SYNCHRON LX Systems)	= 3.4

Serum or plasma (in the range of 0.6 to 15.0 mg/dL):

MEAN (SYNCHRON CX7 DELTA) = 3.5
 CORRELATION COEFFICIENT (r) = 0.9987

Y (SYNCHRON LX Systems) = 0.958X - 0.03
 N = 77
 MEAN (SYNCHRON LX Systems) = 3.4
 MEAN (IMAGE[®]) = 3.6
 CORRELATION COEFFICIENT (r) = 0.9959

Refer to References (15) 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 PRECISION VALUES

TYPE OF PRECISION	SAMPLE TYPE	1 SD		CHANGEOVER VALUE ^d		% CV
		mg/dL	mg/L	mg/dL	mg/L	
Within-run	Serum/Plasma	0.2	2.0	4.0	40.0	5.0
	Serum/Plasma (ORDAC)	NA ^e	NA	NA	NA	10.0
Total	Serum/Plasma	0.3	3.0	4.0	40.0	7.5
	Serum/Plasma (ORDAC)	NA	NA	NA	NA	15.0

Comparative performance data for a SYNCHRON LX[®] System evaluated using the NCCLS Proposed Guideline EP5-T2 appears in the table below.¹⁶ Each laboratory should characterize their own instrument performance for comparison purposes.

TABLE 8 NCCLS EP5-T2 PRECISION ESTIMATE METHOD

TYPE OF IMPRECISION	SAMPLE TYPE		No. Systems	No. Data Points ^f	Test Mean Value (mg/dL)	EP5-T2 Calculated Point Estimates	
						SD	%CV
Within-run	Serum	Control 1	1	80	1.33	0.05	3.46
	Serum	Control 2	1	80	4.85	0.05	1.11
	Serum	Control 3	1	80	7.49	0.06	0.79
Total	Serum	Control 1	1	80	1.33	0.05	3.96
	Serum	Control 2	1	80	4.85	0.07	1.40
	Serum	Control 3	1	80	7.49	0.10	1.32

NOTICE

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

ADDITIONAL INFORMATION

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

SHIPPING DAMAGE

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

REFERENCES

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ENDNOTES

- a Data shown was collected using SYNCHRON CX Systems. Equivalency between SYNCHRON LX Systems has been established by Deming regression analysis to SYNCHRON CX Systems.
- b Data shown was collected using SYNCHRON CX Systems. Equivalency between SYNCHRON LX Systems has been established by Deming regression analysis to SYNCHRON CX Systems.
- c NSI = No Significant Interference (within ± 0.4 mg/dL or 10%).
- d 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.
- e NA = Not applicable.
- f The point estimate is based on the 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.