

## Intended Use

For the quantitative determination of C-reactive protein in serum or plasma by latex particle enhanced immunoturbidimetric assay using the Yumizen C560 analyzer.  
**Rx Only.**

## Introduction

C-reactive protein (CRP) is an acute phase protein that is involved in the activation of complement, acceleration of phagocytosis, and detoxification of substances released from damaged tissue. As such, CRP is considered to be one of the most sensitive indicators of inflammation. In response to an inflammatory stimulus, a rise in CRP may be detected within 6 hours. CRP is a sensitive, though considered to be a non-specific indicator of acute phase reactants.<sup>1, 2, 3</sup> Measurement of C-reactive protein is most frequently used for the evaluation of injury to body tissues or, for the detection of an inflammatory event somewhere in the body. CRP levels in serum are typically elevated in patients with arthritis or liver disease such as hepatitis A, hepatitis B, or biliary cirrhosis, and after severe infections such as septic shock.

The CRP-HS is intended for the quantitative determination of human CRP by latex particle enhanced immunoturbidimetric assay (ITA). ITA methods for quantitative determination of antibody and antigen immunoprecipitation complexes have been described.<sup>4, 5, 6, 7</sup>

## Principle of the Test

Latex particles coated with antibody specific to human CRP aggregate in the presence of CRP from the sample forming immune complexes. The immune complexes cause an increase in light scattering which is proportional to the concentration of CRP in the serum. The light scattering is measured by reading turbidity (absorbance) at 570 nm. The CRP concentration is determined from a calibration curve developed from CRP standards of known concentration.

## Reagents

R-1: Buffer Reagent: Glycine buffer: 170 mM

R-2: Latex Suspension: Latex particles coated with rabbit anti-human CRP antibodies: 0.20% (w/v)

## Reagent Preparation

Reagents are ready to use and do not require reconstitution. Mix gently before using.

## Reagent Storage and Stability

1. All reagents should be stored at 2-8°C and protected from light. Unopened reagents can be used until the expiration date on the package and bottle labels.
2. Once the reagent vial has been opened, store tightly capped at 2-8°C and use within 1 month.

## Precautions and Hazards

1. For *in vitro* diagnostic use only. Not to be used internally in humans or animals. Normal precautions for handling laboratory reagents should be followed.
2. Do not mix or use reagents from one test kit with those from a different lot number.
3. Do not use reagents past their expiration date stated on each reagent container label.
4. Do not pipette by mouth. Avoid ingestion and contact with skin.
5. Reagents in this kit contain <0.1% (w/v) sodium azide as a preservative. Sodium azide may form explosive compounds in metal drain lines. When disposing of reagents through plumbing fixtures, flush with copious amounts of water.
6. All specimens, controls and calibrators should be handled as potentially infectious, using safe laboratory procedures (NCCLS M29-T2).<sup>8</sup>

## Hazards:

**R1 and R2: Hazard Classifications:** Not a hazardous substance or mixture.

**Pictogram:** Not required.

**Signal Word:** Not required.

**Hazard Statements:** Not a hazardous substance or mixture.

**Precautionary Statements:** Not a hazardous substance or mixture.

**Refer to the Safety Data Sheet for this product (SDS-C7568) available by calling 1-734-487-8300.**

## Specimen Collection and Storage

1. Freshly drawn serum is preferred and should be used within the day of collection. Samples may also be stored refrigerated (2-8°C) for one week or at -30°C for up to 1 year. Use undiluted samples for this assay.
2. Lithium heparin or EDTA plasma samples may also be used.
3. Use plastic tubes for storing the sample, do not use glass.
4. Collect specimens per NCCLS document H4-A3.<sup>9</sup>

## Interference

1. All interference studies were performed according to the procedures recommended in NCCLS guideline No. EP7-P for interference testing in clinical chemistry.<sup>10</sup>
2. Hemoglobin to 500 mg/dl, Lipid to 900 mg/dl, Bilirubin to 30 mg/dl and RF to 560 IU/ml were found not to interfere with this assay.
3. Dust particles or other particulate matter in the reaction solution may result in extraneous light-scattering, which may affect the accuracy of this test.
4. See Young, et al for other interfering substances.<sup>11</sup>

## Materials Supplied

1. Reagent 1 (R-1) Buffer Reagent
2. Reagent 2 (R-2) Latex Suspension

# Pointe C-Reactive Protein High Sensitivity CRP (HS) Wide Range Reagent Set

## Materials Required But Not Supplied

1. Yumizen C560 Analyzer
2. Yumizen C560 Operation manual
3. Multi-point calibrators: CRP Multi-Calibrator Set, catalog number C7568-CAL.
4. CRP control Set, catalog number C7568-CTL
5. Isotonic saline

## Calibration Curve

It is recommended that a multi-point calibration curve be developed using a CRP Multi-standard Set. It is recommended that the user determine calibration frequency as this will depend on the instrument and type/number of other assays being run. Initially, calibration should be performed each day. Calibration stability studies have shown the calibration curve will be stable for at least 14 days.

## Quality Control

It is recommended that commercially available control serum with known concentrations of CRP be included in all assay runs. Levels in the range of 2.5 mg/L and 55.0 mg/L are recommended. Quality control requirements should be performed in conformance with local, state, and/or Federal regulations or accreditation requirements.

## Limitations of the Procedure

1. The CRP-HS has a measurable range from 0.1 to 320.0 mg/L using the manufacturer's CRP Multi-Calibrator Set and the correct instrument parameters.
2. Reagents should not be used after the expiration date indicated on the kit label. Do not mix reagents with different lot numbers.
3. If the CRP concentration is greater than highest calibrator value, dilute one part sample with four parts isotonic saline and re-assay. Multiply results by 5 to compensate for the dilution.

## Expected Values

Expected value for CRP in healthy individuals is below 3.0 mg/L.<sup>13</sup> It is recommended that each laboratory establish its own expected range.

## Performance

1. Assay Range: 0.1-320.0 mg/L.
2. Correlation: A study was performed between the Yumizen C560 and a similar analyzer using this method, resulting in the following:

Method	CRP
N	99
Mean CRP (mg/L)	27.33
Range (mg/L)	0.0-311.6
Standard Deviation	59.84
Regression Analysis	$y = 1.055x - 0.96$
Correlation Coefficient	0.9980

3. Precision: Precision studies were performed following a modification of the guidelines contained in the NCCLS document EP5-T2.<sup>12</sup>

Sample	Within Day			Total		
	LOW	MID	HIGH	LOW	MID	HIGH
N	20	20	20	40	40	40
Mean	2.17	48.04	165.09	2.20	49.31	162.61
Standard Deviation	0.05	0.15	1.11	0.11	2.46	2.89
Coefficient of Variation (%)	2.2%	0.3%	0.7%	4.8%	5.0%	1.8%

4. Sensitivity: 2SD limit of detection (95% Conf) = 0.1 mg/L

The following performance data was obtained using a Hitachi 717 analyzer and standard protocol.

5. Specificity: When serum containing a known level of CRP (2.5 mg/L) is measured, the assay value obtained is within  $\pm 10\%$ .

## References

1. Osmond, A.P., et al, *Proc. Natl. Acad. Sci.* 74:739-743, 1977.
2. Pepys, M.B. *Lancet.* 1:653-657, 1981.
3. Schultz, D.R. and P.I. Arnold. *Semin. Arthritis Rheum.* 20 (3):129-147, 1990.
4. Killingsworth, L.M. and J. Savory. *J. Clin. Chem.* 19:403-407, 1973.
5. Lizana, J. and K. Helling. *Clin. Chem.* 20:1181, 1974.
6. Otsuji, S., et al, *Clin. Chem.* 28:2121-2124, 1982.
7. Malkus, H., et al, *Clinica Chimica Acta*, 88:523-530, 1978.
8. NCCLS document, "Protection of Laboratory Workers from Infectious Disease Transmitted by Blood, Body Fluids, and Tissue", 2<sup>nd</sup> Ed. (1991).
9. NCCLS document, "Procedures for the Collection of Diagnostic Blood Specimens by Skin Puncture", 3<sup>rd</sup> Ed. (1991).
10. NCCLS document, "National Evaluation Protocols for Interference Testing", Evaluation Protocol Number 7, Vol. 4, No. 8, (June 1984).
11. Young, D.S., et al, *Clin Chem* 21:1D, 1975.
12. NCCLS document, "Evaluation of Precision Performance of Clinical Chemistry Devices", 2<sup>nd</sup> Ed. (1992)
13. Liuzzo, G., et al, *N Eng J Med*, 331:417-424, 1994.
14. U.S. Patent nos. 6,248,597; 6,828, 158.

**CHEMISTRY PARAMETERS**

Chem:	CRP	No.:	214	Sample Type:	Serum	
Chemistry:	CRP			Print Name:	CRP	
Reaction Type:	End Point			Reaction Direction:	Positive	
Pri Wave:	570			Sec Wave:		
Unit:	mg/L			Decimal	0.1	
Blank Time:	47	49		Reaction Time:	80	82
	Sample Vol.	Aspirated	Diluent	Reagent Vol.	Diluent	
Standard:	4.7 UI	--- ul	--- ul	R1:	120 ul	--- ul
Decreased:	4.7 UI	30 ul	120 ul	R2:	120 ul	-- ul
Increased:	--- UI	--- ul	--- ul	R3:	--- ul	-- ul
	<input type="checkbox"/> Sample Blank	<input checked="" type="checkbox"/> Auto Rerun		R4:	--- ul	--- ul
<b><u>Slope/Offset Adjustment</u></b>						
	Slope: 1	Offset: 0				

Linearity Range (Standard)	0.1	320	Linearity Limit:
Linearity Range (Decreased)	---	---	Substrate Depletion:
Linearity Range (Increased)	---	---	Mixed Blank Abs:
R1 Blank Abs:	---	---	Uncapping Time
Blank Response:	---	---	Reagent Alarm Limit:
Twin Chemistry:			<input type="checkbox"/> Enzyme Linear Extension
<input type="checkbox"/> Prozone Check		<input type="radio"/> Rate Check	<input type="radio"/> Antigen Addition
Q1:	Q2:	Q3:	Q4:
PC:	ABS:		

# Pointe C-Reactive Protein High Sensitivity CRP (HS) Wide Range Reagent Set

## CALIBRATION PARAMETERS

<b>Calibrator Definition</b>						
Calibrator:	*	Lot No.:			*	
Exp Date:	*					
<b>Carousel</b>	<b>Pos</b>					
Sample Carousel 1	*					
Sample Carousel 2						
Sample Carousel 3						
<b>Reagent/Calibration</b>						
<u>Calibrator</u>	<u>Pos</u>	<u>Lot No</u>	<u>Exp Date</u>	<u>Chem</u>	<u>Conc</u>	<u>Unit</u>
Water	W	*	*	CRP	*	mg/L
CRP Cal 1	*	*	*	CRP	*	mg/L
CRP Cal 2	*	*	*	CRP	*	mg/L
CRP Cal 3	*	*	*	CRP	*	mg/L
CRP Cal 4	*	*	*	CRP	*	mg/L
CRP Cal 5	*	*	*	CRP	*	mg/L
<b>Calibration Setup</b>						
Chem:	CRP					
<u>Calibration Settings</u>						
Math Model:	Spline					
Factor:	Replicates:		2			
<u>Acceptance Limits</u>						
Cal Time:	336	Hour				
Slope Diff:	---	SD:	---			
Sensitivity :	---	Repeatability:	---			
Deter Coeff:	---					
<u>Auto Calib.</u>						
<input type="checkbox"/> Bottle Changed	<input type="checkbox"/> Lot Changed	<input type="checkbox"/> Cal Time				

It is recommended that two levels of control material be assayed daily.  
\* Indicates user defined parameter.

**REF** 14-C7568-480



Manufactured by  
HORIBA Instruments Incorporated-Pointe Brand  
5449 Research Drive Canton, MI 48188



### Certified to Perform Reagents

The Pointe reagents are certified to be manufactured according to specified parameters. Any Pointe reagent product not meeting specifications through its listed expiration date will be remedied immediately without charge.

Manufactured by HORIBA Instruments Incorporated – Pointe Brand  
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### Symbol Key

Use by (YYYY-MM-DD)	<b>LOT</b> Lot and batch code	<b>REF</b> Catalog number
Manufacturer	Temperature limitation	Consult instructions for use
<b>IVD</b> <i>In vitro</i> diagnostic medical device <b>Rx Only</b> : Prescription Use Only		