



TECO DIAGNOSTICS

1268 N. Lakeview Ave.
Anaheim, CA 92807
1-800-222-9880

CRP TURBI WR REAGENT

TC MATRIX-240/480

INTENDED USE

Test for the quantitative immunological determination of C- reactive protein in human serum and plasma.

SUMMARY AND PRINCIPLE^{1, 2, 3, 4, 5}

In 1930, Tillet and Francis identified a substance in the sera of acutely ill patients that bound cell wall C- polysaccharide of *Streptococcus pneumoniae* and agglutinates the organisms.¹ In 1941 the substance was shown to be a protein and named C-reactive protein (CRP).² CRP is composed of five identical, non-covalently associated, non-glycosylated subunits of 23 kDa to form a disk-shaped structure with radial symmetry and total mass of approximately 115 kDa.³ It is an acute phase reactant produced by the liver in response to inflammatory cytokines, most prominently interleukin-6.^{4,5,6} It also helps non-specific host defense against infectious organisms by activating the classical complement pathway³ and can bind to phagocytic cells.⁶

CRP is one of the most potent acute phase reactants, and plasma concentrations increase up to 1000-fold after myocardial infarction, stress, trauma, infection, inflammation, surgery or neoplastic proliferation,⁷ and is normally present in plasma at a concentration below 5 mg/L. Concentrations higher than 5 to 10 mg/L suggest the presence of an infection or inflammatory process. Concentrations are usually higher in bacterial infection than in viral infection, but concentrations greater than 100 mg/L can be seen in uncomplicated influenza and infectious mononucleosis. The increase with inflammation occurs within 6 to 12 hours and peaks at about 48 hours and is usually proportional to the extent of tissue damage. However, since the increase is non-specific, it cannot be interpreted without other clinical information.³

A systematic review and meta-analysis reported that CRP has an estimated diagnostic sensitivity of 75% and specificity of 67% in distinguishing bacterial infection from non-infectious inflammation causes.⁵

Another study found that in pediatric patients with a systemic inflammatory response, the use of a panel of eight biomarkers, including CRP and procalcitonin, had a negative predictive value of 90% in identifying patients without bacterial infection.⁸

CRP is frequently used to diagnose bone and joint infections in both children and adults.^{9,10} It is also used as a marker for the timing of transition to oral antibiotic therapy in the treatment of bone and joint infections in children.^{11,12} Although some studies have concluded that CRP can be used to safely guide and reduce antibiotic use in the treatment of acute exacerbation of chronic obstructive pulmonary disease, these results have not yet come into use in clinical practice outside of these study settings.^{13,14,15} There are also some studies on the appropriateness of deciding on the continuation of antibiotic use during bacteremia treatment guided by CRP results.^{12,16}

Epidemiologic studies show that mildly elevated CRP concentrations are associated with cardiovascular disease (CVD) risk.¹⁷ Increased concentrations may reflect low- grade, chronic intimal inflammation; but the use of CRP in CVD requires the use of a test with detection limits below 0.3 mg/L, often referred to as a high-sensitivity CRP assay.³

TEST PRINCIPLE

immunoturbidimetric Measurement

The test aims to detect an antigen-antibody reaction between a polyclonal, a monoclonal and specific Anti-CRP antibody with the CRP antigen in the samples.

The CRP concentration in the sample is quantified by turbidimetric measurement of the turbidity of this antigen- antibody complex at a wavelength of 572 nm.

REAGENTS

Each kit contains:

Reagent 1:

Glycine buffer 0.12 mol/L
Sodium azide 0.1%
pH 8.6

Reagent 2:

Anti- CRP antibodies
Sodium azide 0.1%

REAGENT PREPARATION

Reagents are ready for use.

WARNINGS AND PRECAUTIONS

IVD: For in Vitro Diagnostic use only. Do not use expired reagents. Reagents with two different lot numbers should not be interchanged.

For professional use.

Follow Good Laboratory Practice (GLP) guidelines. Contains sodium azide.

CAUTION: Human source samples are processed with this product. All human source samples must be treated as potentially infectious materials and must be handled in accordance with OSHA standards.

REAGENT STORAGE AND STABILITY⁶

Reagents are stable at 2-8°C until the expiration date stated on the label which is only for closed vials.

Once opened vials are stable for 30 days at 2-8°C in optimum conditions. On board stability is strongly related to auto analyzers' cooling specification and carry-over values.

Reagent stability and storage have been verified by using Clinical and Laboratory Standards Institute (CLSI) EP25-A protocol.

SAMPLE REQUIREMENTS

Serum and plasma collected by standard procedure can be used. For plasma, specimen collection tubes with Li heparin, K2 EDTA, K3 EDTA can be used. Multiple sample freezing and thawing should be avoided.

CRP activity stability in serum and Li-heparinized plasma:

2 weeks at 20-25°C
3 weeks at 2-8°C
1 year at -20°C

CRP activity stability in K2 EDTA and K3 EDTA plasma:

1 day at 20-25°C
3 weeks at 2-8°C
1 year at -20°C.

MATERIAL REQUIRED BUT NOT PROVIDED

1. CRP Turbi WR calibrator
2. At least two levels of control materials

PROCEDURE

For TC-MATRIX-240

Test Name:	CRP TURBI	R1:	75
Full Name:	CRP TURBI WR	R2:	75
Pri. Wave:	578 nm	SAMPLE VOLUME:	2.0
Sec. Wave:	/	Calibration Type:	Spline
Assay/ Point:	Fix-time	K Value:	/
Start - End:	18 - 30	Point:	5

Decimal place:	1	Blank Type:	Reagent
Unit:	mg/L	Point 0 (Blank) Con.:	0.0
Linearity Range:	2 - 300	Point 1 (CAL) Con.:	
Correlation Factor:	1.0000 - 0.0000	Point 2 (CAL) Con.:	
		Point 3 (CAL) Con.:	
		Point 4 (CAL) Con.:	

For TC-MATRIX-480

Test Name:	CRP TURBI	R1:	80
Full Name:	CRP TURBI WR	R2:	80
Pri. Wave:	578 nm	SAMPLE VOLUME:	2.0
Sec. Wave:	/	Calibration Type:	Spline
Assay/ Point:	Fix-time	K Value:	/
Start - End:	18 - 30	Point:	5
Decimal place:	1	Blank Type:	Reagent
Unit:	mg/L	Point 0 (Blank) Con.:	0.0
Linearity Range:	2 - 300	Point 1 (CAL) Con.:	
Correlation Factor:	1.0000 - 0.0000	Point 2 (CAL) Con.:	
		Point 3 (CAL) Con.:	
		Point 4 (CAL) Con.:	

CALIBRATION AND QUALITY CONTROL

Calibration: The assay requires the use of an CRP Turbi WR Calibrator.

Calibration stability is 30 days. Calibration stability depends on the application characteristics and cooling capacity of the autoanalyzer used.

Control: Commercially available control material with established values determined by this method can be used.

At least two level controls must be run once in every 24 hours. Each laboratory should determine its own quality control scheme and procedures. If quality control results are not within acceptable limits, calibration is required.

REFERENCE RANGE

Serum and plasma³¹: <5.0 mg/L (<0.5 mg/dL)

Each laboratory should investigate the transferability of the expected values to its own patient population and if necessary, determine its own reference range.

Note:

1. Concentrations of some biochemical markers, including CRP, increase early in extrauterine life, reflecting maternal concentrations, but then begin to fall during the first 2 weeks of life.¹⁹
 2. Individuals living at high altitude may have higher CRP concentrations. Adaptation can take weeks when returning to normal altitude.^{20,21}
- Reference interval has been verified by using CLSI EP28- A3c protocol.²²

Unit Conversion:

CRP mg/dL x 10 = CRP mg/L

PERFORMANCE CHARACTERISTICS

Measuring Interval

According to CLSI EP34-ED1:2018, "Measuring Interval" refers to the interval where the analyte concentration is measured with intended accuracy in terms of medical and laboratory requirements without dilution, concentrating or any kind of pre-treatment that is between the analyte's lower limit of quantitation (LLOQ) and upper limit of quantitation (ULOQ).²³

Linearity

The determined analytic measuring interval for CRP Turbi WR is 2-300 mg/L.

Limit of Detection (LoD): The limit of detection is 0.5 mg/L.

Limit of Quantitation (LoQ): 2.0 mg/L.

Note: LoQ values are based on Coefficient of Variation Percentage (CV) % ≤20.

LoD and LoQ values have been verified by using CLSI EP17-A2 protocol.²⁴

Precision

Running system has been developed according to 20x2x2 "The Single Site" protocol. Repeatability and Within- Laboratory Precision/Within-Device values have been obtained according to the running results.

According to the protocol in use, 2 separate runs per day have been made for 20 days (no obligation for being consecutive days). This protocol has been applied to each low and high samples separately and 80 results have been obtained for each one. Statistically, the results have been obtained using 2-factor Nested-ANOVA model.²⁷

Repeatability (Within Run) and Repeatability (Day to Day) SD and CV% values of CRP Turbi WR have been given in table 1 and 2 respectively.

Table 1. CRP Turbi WR Repeatability (Within Run) results obtained from samples in two different concentrations

Mean Concentration	SD*	CV%	n
10.0 mg/L	0.26	2.60	80
30.0 mg/L	0.20	0.67	80

*SD: Standard Deviation

Note: This working system has been named "Within-Run Precision" in the previous CLSI - EP05-A2 manual.²⁷

Table 2. CRP Turbi WR Repeatability (Day to Day) results obtained from samples in two different concentrations

Mean Concentration	SD	CV%	n
10.0 mg/L	0.47	4.70	80
30.0 mg/L	1.11	3.70	80

Note: This working system has been named "Total Precision" in the previous CLSI - EP05-A2 manual.²⁷

Precision Studies data have been verified by using CLSI EP05-A3 protocol.²⁶

Prozone Effect: No prozone effect has been observed up to 400 mg/L value which is tested for CRP Turbi WR.

Interference

Endogenous interferant and analyte concentrations that have been used in the CRP Turbi WR scanning tests has been determined according to "CLSI EP37-ED1:2018" and "CLSI EP07-ED3:2018" manuals.^{28,29}

The total acceptable error rate, which is going to be used to detect whether the observed differential value obtained from CRP Turbi WR interference scanning test is appropriate, is determined as ±10%.³⁰

In CRP Turbi WR test results, no significant interaction has been observed in the determined endogenous interferant and analyte concentrations or between interferants and analyte.

Interferent and Concentration	CRP Turbi WR Target (mg/L)	N*	Observed Recovery%
Bilirubin Total 4.86 mg/dL	15.3	*3	106
Bilirubin Total 4.60 mg/dL	40.5	*3	110
Triglyceride 2128 mg/dL	14.5	*3	98

Triglyceride 2025 mg/dL	47.4	*3	99
Hemoglobin 720 mg/dL	15.5	*3	98
Hemoglobin 990 mg/dL	48.3	*3	104

* Total acceptable error rate determined as interference limit and repeatability (within run) pre-detected for the related method were used for the calculations of how many times the control and test samples prepared as a serum pool are going to be run repetitively. In the calculations, the accepted error rate for type 1 (α error) was 5% and for type 2 (β error) was 10% (90% power).²⁹

It should be noted that endogenous interferants, as well as various medicines and metabolites, anticoagulants (e.g. Heparin, EDTA, citrate, oxalate) and preservatives (e.g. sodium floride, iodoacetate, hydrochloride acid) such as additives, materials that may contact samples during collection and processing (serum separator devices, sample collection containers and contents, catheters, catheter wash solutions, skin disinfectants, hand cleaners and lotions, glass washing detergents, powder gloves), dietary substances known to affect some specific tests (caffeine, beta-carotene, poppy seeds, etc.), or some substances present in a sample that cause foreign proteins (heterophilic antibodies, etc.), autoimmune response (autoantibodies, etc.), or due to malignancy (for example, interference by paraproteins with phosphate testing and indirect ion selective electrode methods) may show some negative effects that will cause various attempts and some misjudgements.²⁹

These performance characteristics have been obtained using an autoanalyzer. Results may vary slightly when using different equipment or manual procedures.

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TECO DIAGNOSTICS
1268 N. Lakeview Ave.
Anaheim, CA 92807
U.S.A.
Website: www.tecodiagnostics.com