

**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY TEMPLATE**

A. 510(k) Number:

k083040

B. Purpose for Submission:

New device

C. Measurand:

C Reactive Protein (CRP)

D. Type of Test:

Quantitative – latex immunoturbidimetric

E. Applicant:

Alfa Wassermann Diagnostic Technology, Inc.

F. Proprietary and Established Names:

S-Test C Reactive Protein (CRP) Reagent cartridge

G. Regulatory Information:

Product Code	Classification	Regulation Section	Panel
DCN – C Reactive Protein	Class II	21 CFR§ 866.5270	75 Chemistry

H. Intended Use:

1. Intended use(s):

See indications for use below

2. Indication(s) for use:

The S-Test C-Reactive Protein Reagent is intended for the quantitative determination of C-reactive protein concentration in serum or heparin plasma using the S40 Clinical Analyzer. Measurement of C-reactive protein aids in

evaluation of the amount of injury to body tissues. This test is intended for use in clinical laboratories or physician office laboratories. For *in vitro* diagnostic use only

3. Special conditions for use statement(s):

For prescription use only

This test is not intended for high sensitivity CRP measurements.

4. Special instrument requirements:

S40 Clinical Analyzer

I. Device Description:

The S-Test C-Reactive Protein (CRP) device is a single use plastic cartridge composed of two individual reagents in separate wells, a reaction well with a photometric cuvette, and a bar code label which provides all the chemistry parameters, calibration factors, and product information for the instrument. The two reagent wells contain the following materials: (1) 2 amino-2 hydroxymethyl-1,3 propanediol in buffer and (2) anti-human c-reactive protein mouse monoclonal antibody coated latex particles.

J. Substantial Equivalence Information:

1. Predicate device name(s):

Olympus AU640 Clinical Chemistry Analyzer, CRP Latex Test

2. Predicate 510(k) number(s):

k961274

3. Comparison with predicate:

Similarities		
Item	S-Test CRP Reagent	CRP Latex Test
Sample type	Serum or lithium heparin plasma	Serum or lithium heparin plasma
Principle	Latex immunoturbidimetry	Latex immunoturbidimetry
Reaction type	Endpoint	Endpoint

Differences		
Item	S-Test CRP Reagent	CRP Latex Test
Indications for Use	<p>Intended for the quantitative determination of C-reactive protein concentration in serum or heparin plasma using the S40 Clinical Analyzer. Measurement of C-reactive protein aids in evaluation of the amount of injury to body tissues.</p> <p>This test is not intended for high sensitivity CRP measurement</p>	<p>Intended for the quantitative determination of C-reactive protein in serum or plasma on Olympus analyzers. Measurement of CRP is useful for the detection and evaluation of infection, tissue injury, inflammatory disorders and associated diseases. High sensitivity CRP measurements may be useful as an independent marker for recurrent events in patients with stable coronary events or acute coronary syndromes</p>
Instrument	S40 Clinical Analyzer	Olympus analyzers
Measuring Range	5-98 mg/L	1 to 480 mg/L
Detection Limit	2 mg/L	≤ 0.15 mg/L

K. Standard/Guidance Document Referenced (if applicable):

CLSI EP5-A2: Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline-Second Edition (2004)
 CLSI EP10-A: Preliminary Evaluation of Quantitative Clinical Laboratory Methods; Approved Guideline –Second Edition (2002)
 CLSI EP6-A: Evaluation of Linearity of Quantitative Measurement Procedures, A Statistical Approach: Approved Guideline (2003)
 CLSI EP7-A: Interference Testing in Clinical Chemistry; Approved Guideline (2002)
 CLSI EP17-A: Protocols for Determination of Limits of Detection and Limits of Quantitation; Approved Guideline (2004)
 CLSI EP9-A2: Method Comparison and Bias Estimation Using Patient Samples; Approved Guideline (2002)

L. Test Principle:

S-Test CRP – CRP in the sample causes an antigen-antibody reaction with antihuman C-reactive protein mouse monoclonal antibody-coated latex particles, resulting in agglutination. The C-reactive protein concentration is determined by measuring this agglutination by measuring the absorbance change. The rate of increase in absorbance, monitored bi-chromatically at 570 nm/800 nm, is directly proportional to the C-Reactive Protein concentration in the sample.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

Three serum samples (with normal, intermediate and elevated levels) were tested for CRP on two S40 Clinical Analyzers two times per run, two runs per day, for a total of 24 days. The mean, standard deviations, and % coefficients of variation (CV) were calculated for each sample.

<u>Sample 1</u> Mean = 13 mg/L CRP	Within Run	Between Run	Between Day	Total
Coefficient of Variation	3.0%	2.5%	1.7%	4.3%

<u>Sample 2</u> Mean = 29 mg/L CRP	Within Run	Between Run	Between Day	Total
Coefficient of Variation	1.8%	1.8%	1.6%	3.0%

<u>Sample 3</u> Mean = 54 mg/L CRP	Within Run	Between Run	Between Day	Total
Coefficient of Variation	1.1%	0.9%	1.8%	2.3%

In-house precision studies were conducted by testing human serum pools at three levels (normal, intermediate and elevated). The samples were assayed three times a day for five days using one instrument. Precision studies were also conducted at three Physician Office Laboratories (POL) with four trained

operators typically found in these settings. Human serum pools at three concentrations were tested three times a day for five days on four instruments (one at each lab). The results are presented in the table below:

Lab	Sample	Mean	%CV or SD (unit)	
			Within-Run	Total
In-house	1	9	SD 0.4	SD 0.4
			4.8%	4.8%
POL 1	1	9	SD 0.5	SD 0.5
			5.8%	5.8%
POL 2	1	8	SD 0.5	SD 0.5
			6.2%	6.2%
POL 3	1	9	SD 0.6	SD 0.6
			7.5%	7.5%
In-house	2	28	SD 0.8	SD 0.8
			3.0%	3.0%
POL 1	2	29	SD 0.4	SD 0.5
			1.4%	1.8%
POL 2	2	28	SD 0.3	SD 0.5
			1.1%	1.7%
POL 3	2	28	SD 1.4	SD 1.7
			5.1%	6.0%
In-house	3	71	SD 1.4	SD 1.4
			2.0%	2.0%
POL 1	3	75	SD 1.3	SD 1.3
			1.7%	1.7%
POL 2	3	71	SD 0.7	SD 1.1
			1.0%	1.5%
POL 3	3	73	SD 2.2	SD 3.3
			3.0%	4.4%

b. Linearity/assay reportable range:

The reportable range is 5 to 98 mg/L. The assay is linear from 5 to 98 mg/L on the S40 Clinical Analyzer. If a sample result is less than 5 mg/L, the result is flagged by the analyzer as <5 mg/L. If a sample result exceeds 98 mg/L, the result is flagged by the analyzer as >98 mg/L. This range is supported by the limit of detection study (section M.1.d below), the method comparison (section M.2.a below), and the linearity study shown below.

Linearity across the assay range was confirmed by testing commercial linearity standards at 12 levels ranging from 4.9 mg/L to 98.5 mg/L. Each level was tested in replicates of four. The percent recoveries ranged from 95.7 to 106.1%. The linear regression equation obtained for the study was $y = 1.035x - 0.160$, $r^2 = 0.9982$

c. Traceability, Stability, Expected values (controls, calibrators, or methods):

The S Test-CRP cartridges are factory calibrated and traceable to the Institute for Reference Material and Measurement (IRMM) Standard Reference Material CRM470. The 2-D barcode printed on each cartridge provides the analyzer with lot-specific calibration data.

d. Detection limit:

The Limit of Blank and Limit of Detection were determined by assaying low samples (5 serum samples were used) and blank samples (bovine serum albumin in saline). Both the low samples (60 reps, 20 reps per day) and the blanks were assayed each day (5 different samples, 4 reps on 3 days, total n = 60 low samples and 60 blank samples). The testing was split between two instruments. The limit of detection was determined to be 2 mg/L. The assay reportable range is from 5 to 98 mg/L on the S40 Clinical Analyzer. If a sample result is less than 5 mg/L, the result is flagged by the analyzer as <5 mg/L. If a sample result exceeds 98 mg/L, the result is flagged by the analyzer as >98 mg/L.

e. Analytical specificity:

Interference studies to determine the effects of Unconjugated Bilirubin, Hemolysis and Lipemia were performed. Serum pools containing 8 mg/L CRP and 21 mg/L CRP were spiked with various concentrations of unconjugated bilirubin (1.6 - 50 mg/dL), hemoglobin (31-1000 mg/dL) and Intralipid (63 - 2000 mg/dL). The sponsor states that interference is considered to be significant if the analyte recovery changes by more than $\pm 10\%$. There was no significant interference observed from bilirubin, lipemia, or hemolysis at the tested concentrations.

f. Assay cut-off:

Not applicable

2. Comparison studies:

a. Method comparison with predicate device:

A series of 95 serum specimens with CRP values ranging from 5 to 91 mg/L were assayed in singlicate on the S40 Clinical Analyzer using S-Test CRP Reagent and Olympus AU640 Analyzer as the reference method. Least-squares regression analysis (Deming) yielded the following results:

Regression Equation	$y = 0.982x + 1.0$
Correlation Coefficient	0.9945
Std. Error Est.	2.1
Confidence Interval Slope	0.961 to 1.012
Confidence Interval Intercept	0.4 to 1.6

Point of Care in Physician's Office Laboratories

Performance for the S-Test CRP was evaluated at three Physician Office Laboratories and with a total of three operators. Operators assayed unaltered clinical serum samples with values ranging from 5 - 88 mg/L. The correlation study between the device and the predicate for serum yielded the following results.

Lab	1	2	3
N	43	42	43
Range (mg/L)	6 -87	7 - 88	5 - 84
Regression equation	$y = 0.959x + 0.7$	$y = 0.966x + 1.4$	$Y = 0.958x + 0.6$
Correlation coefficient	0.9979	0.9978	0.9971
Standard error	1.5	1.5	1.6
Confidence interval slope	0.939 to 0.979	0.945 to 0.986	0.934 to 0.981
Confidence interval intercept	0.0 to 1.3	0.7 to 2.1	-0.1 to 1.3

b. Matrix comparison:

A study was performed on the S40 by running CRP determinations on 22 paired samples drawn from the same patients in serum and heparin plasma tubes at four POL labs and at a clinical laboratory. The serum results ranged from 7 to 96 mg/L. Six samples were spiked. Least-squares regression analysis (Deming) yielded the following results (serum - x, plasma - y):

Regression Equation	$y = 1.019x - 0.5$
Correlation Coefficient	0.9985
Std. Error Est.	1.6
Confidence Interval Slope	0.994 to 1.045
Confidence Interval Intercept	-1.6 to 0.5

3. Clinical studies:

a. *Clinical Sensitivity:*

Not applicable

b. *Clinical specificity:*

Not applicable

c. Other clinical supportive data (when a. and b. are not applicable):

Not applicable

4. Clinical cut-off:

Not applicable

5. Expected values/Reference range:

CRP: < 10 mg/L

Referenced from: Tietz, N.W. (Ed.), Clinical Guide to Laboratory Tests, 3rd Edition, W.B. Saunders Co., Philadelphia, PA (1995).

The S-Test CRP assay is not intended for high sensitivity CRP (hsCRP) measurements.

N. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

O. Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.