Optilite C-Reactive Protein Reagent, Calibrator and Controls
510(k) Summary

A. 510(k) Number:

K172868

B. Purpose for Submission:

New device

C. Measurand:

C-Reactive Protein

D. Type of Test:

Quantitative immunoturbidimetry

E. Applicant:

The Binding Site

F. Proprietary and Established Names:

Optilite® C-Reactive Protein Reagent,
Optilite® C-Reactive Protein Calibrator,
Optilite® C-Reactive Protein Controls.

G. Regulatory Information:

1. Regulation section:

   21 CFR 866.5270, C-reactive protein immunological test system.

2. Classification:

   Class II

3. Product code:

   DCN, System, Test, C-Reactive Protein

4. Panel:

   Immunology (82)

H. Intended use:

1. Intended use(s):

The Optilite C-Reactive Protein Reagent is intended for the quantitative in vitro determination of C-reactive protein (CRP) concentration in serum using the Binding Site Optilite analyser. Measurement of C-Reactive Protein aids in evaluation of the amount of injury to body tissues and for evaluation of infection, tissue injury, and inflammatory disorders. This test should be used in conjunction with other laboratory and clinical findings.

The Optilite C-Reactive Protein Calibrator is intended for the calibration of the Optilite C-Reactive Protein Reagent on the Optilite analyser.

The Optilite C-Reactive Protein Controls are intended for use in quality control by monitoring accuracy and precision for the Optilite C-Reactive Protein Reagent.

2. Indication(s) for use:

Same as Intended use(s).

3. Special conditions for use statement(s):

Prescription use only

4. Special instrument requirements:

The Binding Site Optilite analyser

I. Device Description:

The Optilite C-Reactive Protein Reagent is comprised of a dual wedge containing the following:

Antiserum: Supplied in stabilised liquid form. Preservatives: 0.099% sodium azide, TRIS pH 8.0.
Reaction Buffer: Containing 0.099% sodium azide, TRIS pH 7.5 as preservatives.

The Optilite C-Reactive Protein Calibrator is comprised of the following:
Pooled human serum, supplied in stabilised liquid form. Containing 0.099% sodium azide, as preservative.

The Optilite C-Reactive Protein Controls are comprised of the following:
Pooled human serum, supplied in stabilised liquid form. Containing 0.099% sodium azide, as preservative.

J. Substantial equivalence information:

1. Predicate device name(s) and 510(k) number(s):

Roche Diagnostics Tina-Quant C-Reactive Protein Gen. 3 (K083444)

2. Comparison with predicate:

Similarities

Item	Device	Predicate
Intended use	Quantitative in vitro determination of C-reactive protein (CRP).	Same.
Method	Turbidimetry	Same.
Reference Interval	<5mg/L	Same.
Sample type	Serum	Serum (also Li-heparin and EDTA plasma)

Differences

Item	Device	Predicate
Measuring Range	5-285mg/L (neat) 25-1425mg/L (1/5 dilution)	0.3-350mg/L (neat) 0.6-700mg/L (1/2 dilution)
Analyser	Optilite	Hitachi 912, 917, Modular P
Antibody	anti- human CRP (goat)	anti-human CRP (mouse)
Open vial stability	Three months at 2 to 8°C	Not stated.
On board stability	30 days.	84 days opened and refrigerated on the analyser.
Reagent	Antiserum	Latex particles coated with anti-CRP (mouse)
Calibration	6 point, single calibrator diluted on analyser	5 point, single calibrator diluted on analyser
Wavelength	340nm	570nm/800nm
Traceability	DA474	CRM470

K. Standards and Guidance documents referenced:

Guidance for Industry - Review Criteria for Assessment of C - Reactive Protein (CRP), High Sensitivity C-Reactive Protein (hsCRP) and Cardiac C-Reactive Protein (cCRP) Assays Guidance for Industry and FDA Staff

CLSI EP17-A2 Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline – Second Edition

CLSI EP7-A2 Interference Testing in Clinical Chemistry, Approved Guideline - Second Edition

CLSI EP6-A: Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach

CLSI EP5-A3 Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline – Third Edition

L. Test Principle:

The determination of soluble antigen (CRP) concentration by turbidimetric methods involves the reaction with specific antiserum (anti-CRP) to form insoluble complexes. When light is passed through the suspension formed a portion of the light is transmitted and focused onto a photodiode by an optical lens system. The amount of transmitted light is indirectly proportional to the specific protein concentration in the test sample. Concentrations are automatically calculated by reference to a calibration curve stored within the instrument.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

The studies were based on CLSI EP5-A3, where 4 sera samples (targeted to 6.8mg/L, 9.5mg/L, 21.5mg/L and 65.4mg/L) were tested in 2 runs per day (each of the 2 runs in duplicate) over 21 days using 1 reagent lot on 3 analysers. Results met the acceptance criteria for total precision (%CV<10%), within-run precision (%CV<5%), between-run precision (%CV<8%), and between-day precision (%CV<8%).

Sample		1	2	3	4
Mean concentration (mg/L)		6.8	9.5	21.5	65.4
Total precision	SD %CV	0.42 6.2	0.41 4.3	0.55 2.6	2.03 3.1
Within-run precision	SD %CV	0.18 2.7	0.12 1.2	0.22 1.0	0.49 0.7
Between-run precision	SD %CV	0.09 1.4	0.12 1.3	0.18 0.8	0.52 0.8
Between-day precision	SD %CV	0.37 5.4	0.37 3.9	0.47 2.2	1.90 2.9
Between-batch precision	SD %CV	0.06 0.6	0.41 1.9	1.67 2.6	4.24 2.9
Between-instrument precision	SD %CV	0.20 3.0	0.06 0.7	0.17 0.8	1.64 2.5

b. Linearity/assay reportable range:

The studies followed CLSI EP6-A, whereby linearity was assessed across the curve width at the standard sample dilution (1+0).

The acceptance criteria were that the %CV for each sample should be ≤8% and the allowable nonlinearity was 0.5mg/L up to 5mg/L, and ± 10% above 5mg/L.

In order to maintain matrix integrity, any spiking with pure protein was no greater than 30% of the total volume.

A series of 14 samples was tested in 3 replicates. Results met the Acceptance criteria for CV<8%.

% High pool	Mean Result	SD	%CV
100.0%	316.03	0.231	0.1%
90.0%	274.87	1.041	0.4%
80.0%	254.07	1.595	0.6%
70.0%	224.27	1.457	0.6%
60.0%	193.40	1.706	0.9%
50.0%	163.53	0.451	0.3%
40.0%	138.37	0.764	0.6%
30.0%	108.87	0.643	0.6%
20.0%	73.37	0.321	0.4%
10.0%	35.80	0.608	1.7%
2.5%	9.97	0.058	0.6%
1.5%	6.27	0.058	0.9%
1.0%	4.93	0.058	1.2%
0.5%	2.70	0.100	3.7%

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

i) *Traceability*:

The calibration of the assay is traceable to the international reference standard ERM-DA474.

ii) Kit Stability:

Real-time stability – A study to establish shelf-life stability (from the date of manufacture when stored at recommended temperature 2-8°C) of the Optilite CRP Kit is on-going. Currently available data supports a 5-month stability claim.

Open-vial stability - The Optilite CRP Kit reagents can be stored, opened at 2 – 8°C for up to 3 months.

On-board stability – The Optilite CRP Kit reagents can be stored on-board the Optilite Analyser for at least 30 days.

d. Detection limit:

The analytical sensitivity was determined in accordance with CLSI EP17-A2. The Limit of Blank (LoB) was based on 4 serum samples run 5 times per day, over 3 days, on 2 reagent lots to give a total of 60 results per lot. The LoB was estimated for each lot as the 95% percentile of the distribution.

The Limit of Detection (LoD) was based on 4 serum samples run 5 times per day, over 3 days, on 2 reagent lots to give a total of 60 results per lot. The LoD calculation followed parametric analysis.

The LoQ was determined from 4 serum samples targeted to be close to the bottom of the measuring range, tested 5 times per day over 3 days on 2 reagent lots.

For LoB and LoD, the highest result obtained from the two lots tested was taken as the final result (see below):

LoB	LoD	LoQ
1.35mg/L	2.66mg/L	5.0mg/L

e. Analytical specificity:

Interferences were assessed according to CLSI EP7-A2 by testing serum samples with CRP concentrations falling at approximately 9mg/L, 60mg/L and 150mg/L. Each sample was spiked with interfering substances and tested in replicates of 3. For non-interference to be claimed, the mean results from the spiked samples must be within 10% of the mean of the control samples.

Haemoglobin and Bilirubin results: The data demonstrated that the assay was not affected by high levels of the following substances: haemoglobin (5g/L) and bilirubin (200mg/L).

Intralipid and Triglyceride results: The data demonstrated that the assay was not affected by triglyceride (500mg/dL), and intralipid (250mg/dL).

Rheumatoid Factor results: The data demonstrated that the assay was not affected by rheumatoid factor (2417IU/mL).

Drug Interference results: The data demonstrated that the assay was not affected by the 14 therapeutic drugs tested at the concentrations given below.

Drug	Concentration tested
Acetaminophen	1324µmol/L
Acetylsalicylic Acid	3.63mmol/L
Amoxicillin	206µmol/L
Ascorbic Acid	342µmol/L
Caffeine	308µmol/L
Cefotaxime	673µmol/L
Theophylline	222µmol/L
Chloramphenicol	155µmol/L
Cimetidine	79.2µmol/L
Digoxin	7.8nmol/L
Fluconazole	245µmol/L
Ibuprofen	1212.5µmol/L
Penicillin	75mg/L
Phenytoin	198µmol/L

f. Assay cut-off:

Not applicable

2. <u>Comparison studies:</u>

a. Method comparison with predicate device:

A total of 193 serum samples spanning the dynamic range were assayed in singlicate by both the Optilite C-Reactive Protein Kit and the Tina-Quant C-Reactive Protein Gen. 3 assay for use on the Modular P analyser. The samples included 83 normal donors and 110 clinical samples.

Regression statistics are based on the balance of the paired results.

Regression fit	**Regression Equation**	**Slope (95% CI)**	**Intercept (95% CI)**
Weighted Linear	Y = 1.07x + 1.16	1.05 to 1.09	0.84 to 1.48
Passing-Bablok	Y = 1.00x + 5.56	0.98 to 1.03	4.10 to 6.87
Weighted Deming	Y = 1.07 + 1.04	1.05 to 1.09	0.45 to 1.64

98.4% of samples tested gave clinically concordant results on both analysers.

b. Matrix comparison:

None

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:

The reference interval was verified by testing 50 adult donor samples.

Consensus reference interval for adults: <5 mg/L
Reference: Dati F, Schumann G, Thomas L et al. Consensus of a group of professional societies and diagnostic companies on guidelines for interim reference ranges for 14 proteins in serum based on the standardization against the IFCC/BCR/CAP reference material (CRM 470). Eur J. Clin Chem Clin Biochem 1996;34:517-520.

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.