510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY

A. 510(k) Number:

K172868

B. Purpose for Submission:

Previously cleared assay on a new instrument

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 uses:

   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. Indications for use:

   Same as Intended uses

3. Special conditions for use statement:

   Prescription use only

4. Special instrument requirements:

   The Binding Site Optilite analyzer (K110035)

I. Device Description:

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

- Antiserum: Supplied in stabilized 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 stabilized 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 stabilized liquid form. Containing 0.099% sodium azide, as preservative

J. Substantial Equivalence Information:

1. Predicate device name:

   Roche Diagnostics Tina-Quant C-Reactive Protein Gen. 3

2. Predicate 510(k) number:

   K083444

3. Comparison with predicate:

Similarities		
Item	Device: Optilite C-Reactive Protein Reagent	Predicate: Tina-Quant C-Reactive Protein Gen. 3
Intended use	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 analyzer. 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.	Immunoturbidometric assay for the in vitro quantitative determination of CRP in human serum and plasma on Roche automated clinical chemistry analyzers
Method	Turbidimetry	Same
Reference Interval	<5 mg/L	Same

Differences		
Item	Device: Optilite C-Reactive Protein Reagent	Predicate: Tina-Quant C-Reactive Protein Gen. 3
Antibody	Anti-human CRP (goat)	Latex particles coated with anti-human CRP (mouse)
Sample type	Serum	Serum, Li-heparin and EDTA plasma
Measuring Range	5–285 mg/L (neat) 25–1425 mg/L (1/5 dilution)	0.3–350 mg/L (neat) 0.6–700 mg/L (1/2 dilution)
Analyzer	Optilite	Hitachi 912, 917, Modular P
Calibration	6-points single calibrator diluted on analyzer	5-points single calibrator diluted on analyzer
Wavelength	340 nm	570 nm / 800 nm
Traceability	ERM-DA474	CRM470
Open vial stability	Three months at 2 to 8°C	Not stated
On board stability	30 days	84 days opened and refrigerated on the analyzer

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

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 EP07-A2: Interference Testing in Clinical Chemistry; Approved Guideline—Second Edition

CLSI EP06-A: Evaluation of the Linearity of Quantitative Measurement Procedures; A Statistical Approach

CLSI EP05-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:

1. Analytical performance: All results for analytical performance met the sponsor's pre-determined acceptance criteria for each study.

   a. Precision/Reproducibility:

   The studies were based on CLSI guideline EP05-A3, where four serum samples were tested in duplicate per run, two runs per day, over 21 days, using one reagent lot over three analyzers. The between-lot reproducibility was previously demonstrated in K161982. The total SD and CV% calculation was based on the within-run, between-run, and between-day data. The results are shown in the table below:

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

   b. Linearity/assay reportable range:

   A linearity study was performed following CLSI guideline EP06-A. The linearity of this assay was confirmed using 14 serially diluted serum samples over the range of 2.70–316.03 mg/L. The results of weighted linear regression analysis are summarized as follows:

Dilution Range (mg/L)	Slope (95% CI)	Y-Intercept (95% CI)	Correlation R
2.70–316.03	1.01 (0.97–1.05)	-0.06 (-0.40–0.28)	1.00

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 of the Optilite CRP Kit is on-going. Currently available data supports that the reagent is stable for five months from the date of manufacture when stored at recommended temperature of 2–8°C.

Open-vial stability - The Optilite CRP Kit reagents can be stored opened at 2–8°C for up to three 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 guideline EP17-A2. The Limit of Blank (LoB) was determined by testing four native serum samples run five times per day, over three days, using two 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 determined by testing four serum samples run five times per day, over three days, using two reagent lots to give a total of 60 results per lot. The LoD calculation followed a parametric analysis.

The Limit of Quantitation (LoQ) was determined by testing four serum samples targeted to be close to the bottom of the measuring range, each tested five times per day over three days using two reagent lots.

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

Detection Limit	Concentration
LoB	1.35 mg/L
LoD	2.66 mg/L
LoQ	5.00 mg/L

e. Analytical specificity:

Interferences were assessed according to CLSI guideline EP07-A2 by testing serum samples with CRP concentrations falling at approximately 9 mg/L, 60 mg/L and 150 mg/L. Each sample was spiked with interfering substances and tested in replicates of three. Controls were prepared by spiking the same volume of the buffer without interfering substances into the serum samples. Percentage interference was calculated using the mean measurements of the test samples and the controls. A difference between the results within ±10% was considered as absence of interference.

Endogenous Interference: The data demonstrated that the assay was not affected by the levels of the following substances: hemoglobin (5 g/L), bilirubin (200 mg/L), triglyceride (500 mg/dL), intralipid (250 mg/dL), and rheumatoid factor (2417 IU/mL).

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

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

f. Assay cut-off:

Not applicable

2. Comparison studies:

a. Method comparison with predicate device:

A total of 193 serum samples spanning the measuring range were assayed in singlicate by both the Optilite C-Reactive Protein and the Tina-Quant C-Reactive Protein Gen. 3 kits. The samples included 83 normal donors and 110 clinical samples. 80 samples (71 normal donors and 9 clinical samples) were excluded from data analysis due to results reporting as lower than the bottom of the measuring range for the Optilite C-Reactive Protein assay. A total of 113 samples were included in the

comparative data analysis and the result is as follows. Measurement procedure comparison between predicate (x) and test (y) device was evaluated using Passing-Bablok regression analysis.

Method Comparison (n=113)				
Regression Analysis	**Line fit**	**95% CI Slope**	**95% CI Intercept**	**Pearson's r**
Passing-Bablok	y = 1.00x + 5.56	0.98–1.03	4.10–6.87	1.00

b. Matrix comparison:

Not applicable

3. Clinical studies:

a. Clinical Sensitivity, Clinical specificity and Other clinical supportive data:

Not applicable

4. Clinical cut-off**:**

See expected values/reference range.

5. Expected values/Reference range:

The reference interval was verified by testing 50 healthy adult donor samples. Forty-eight (48) of 50 samples tested had concentrations within the consensus reference interval taken from the literature (<5 mg/L).

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.