510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY

A. 510(k) Number:

K162263

B. Purpose for Submission:

New assay

C. Measurand:

Rheumatoid Factor (IgM)

D. Type of Test:

Quantitative immunoturbidimetry

E. Applicant:

The Binding Site, Ltd.

F. Proprietary and Established Names:

Optilite® Rheumatoid Factor Kit

G. Regulatory Information:

1. Regulation section:

   21 CFR § 866.5775: Rheumatoid factor immunological test system

2. Classification:

   Class II

3. Product code:

   DHR: System, test, Rheumatoid Factor

4. Panel:

   Immunlogy (82)

H. Intended Use:

1. Intended use:

   The Optilite Rheumatoid Factor (RF) Kit is intended for the quantitative in vitro measurement of rheumatoid factor in serum using the Binding Site Optilite analyser. Measurement of rheumatoid factor may aid in the diagnosis of rheumatoid arthritis. This test should be used in conjunction with other laboratory and clinical findings.

2. Indication for use:

   Same as Intended Use above.

3. Special conditions for use statement:

   For prescription use only.

4. Special instrument requirements:

   The Binding Site Optilite

I. Device Description:

The Optilite Rheumatoid Factor Kit contains:

Reaction Buffer: Containing glycine buffer (pH 8.3), sodium chloride, sodium ethylenediamine tetra acetric acid disodium salt dehydrate, bovine serum albumin, sodium azide (0.09%,w/v).

Latex Reagent: Containing glycine buffer (pH 7.3), sodium chloride, latex particle adsorbed human IgG, sodium azide (0.09%, w/v).

RF Controls: Supplied at two levels, Low and High. Target values and ranges are supplied in the Quality Control certificate. Supplied ready for use.

RF Calibrator 1–5: Calibration has been carried out and values have been assigned using an immunoturbidimetric method standardized to the international reference preparation, WHO Standard 64/2. Supplied ready for use.

J. Substantial Equivalence Information:

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

   Rheumatoid Factor (RF) Kit for use on SPAPLUS, K160070

2. Comparison with predicate:

Similarities		
Item	**Optilite®RF Kit**	**Predicate**
Intended Use	The Optilite Rheumatoid Factor (RF) Kit is intended for the quantitative in vitro measurement of rheumatoid factor in serum using the Binding Site Optilite analyser. Measurement of rheumatoid factor may aid in the diagnosis of rheumatoid arthritis. This test should be used in conjunction with other laboratory and clinical findings.	The Rheumatoid Factor (RF) Kit for use on SPAPLUS® is intended for the quantitative in vitro measurement of rheumatoid factor in serum using the Binding Site SPAPLUS® analyser. Measurement of rheumatoid factor may aid in the diagnosis of rheumatoid arthritis. This test should be used in conjunction with other laboratory and clinical findings.
Assay type	Quantitative	Same
Specimen Type	Serum	Same
Antibody	Human IgG anti-human-IgM	Same
Intended use	Turbidimetric *in vitro* quantification of rheumatoid factor	Same
Calibration	WHO 64/2	Same
Calibrator	5 levels	Same
Expected value	12.5 IU/mL	Same
RF Control	Two levels	Same
Unopened Kit	12 months	Same
Open Vial Stability	3 months	Same
On-board stability	30 days	Same

Differences		
Item	**RF Kit on SPAPLUS®**	**Predicate**
Instrument	Binding Site Optilite	Binding Site SPAPLUS
Measuring range	7–100 IU/mL (1+0 dilution) 70–1000 IU/mL (1+9 dilution)	10–104 IU/mL (1/1: Standard Dilution) 70–1040 IU/mL (1/10: Automatic reflex dilution on high results at standard dilution)

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

- CLSI EP05-A2, Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline—Second Edition
- CLSI EP6-A, Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach; Approved Guideline
- CLSI EP17-A, Protocols for Determination of Limits of Detection and Limits of Quantitation; Approved Guideline
- CLSI EP07-A2, Interference Testing in Clinical Chemistry; Approved Guideline

L. Test Principle:

The determination of soluble antigen concentration by turbidimetric methods involves the reaction with specific antiserum 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.

M. Performance Characteristics (if/when applicable):

All results from all studies met the manufacturer's pre-specified acceptance criteria.

1. Analytical performance:

   a. Precision/Reproducibility:

   The studies were based on CLSI EP05-A2; five sample preparations were tested in two runs per day (each of the two runs in duplicate) over 21 days using three analysers and three lots for a total of 84 replicates. A summary of the results is shown below. All results are in IU/mL.

RF Sample	Mean	Within-Run		Between-Run		Between-Day		Total Precision	
		SD	%CV	SD	%CV	SD	%CV	SD	%CV
1	12.3	0.30	2.5	0.26	2.2	0.74	6.0	0.84	6.9
2	19.4	0.12	0.7	0.29	1.5	0.71	3.7	0.78	4.0
3	38.1	0.22	0.6	0.50	1.3	1.49	3.9	1.59	4.2
4	75.7	1.26	1.7	0.95	1.3	2.83	3.7	3.24	4.3
5	191.0	2.79	1.5	2.82	1.5	6.11	3.2	7.28	3.8

RF Sample	Mean	Between-lot		Between-instrument	
		SD	%CV	SD	%CV
1	12.3	0.2	1.43	0.52	4.2
2	19.4	0.2	1.08	0.54	2.8
3	38.1	1.2	3.10	0.67	1.8
4	75.7	3.1	4.10	0.74	1.0
5	191.0	5.5	2.87	2.98	1.6

b. Linearity/assay reportable range:

A linearity study was performed following CLSI guideline EP6-A. The linearity of this assay has been confirmed by dilution of serum samples with analyte-depleted serum to cover the range 7–100 IU/mL (total of 9 dilutions). Deviation from linearity calculated according to CLSI guideline EP6-A was ≤ ±5%. The regression equation for the linear range (7–100 IU/mL) was y = 0.999x + 0.04 IU/mL–.

Antigen Excess: No antigen excess was observed up to a level of 59 times the top of the calibration curve at the standard 1+0 sample dilution. This is equivalent to 5900 IU/mL.

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

(i) *Traceability*: The calibration of the assay is traceable to the International Reference Preparation of Rheumatoid Arthritis Serum WHO 64/2.

(ii) *Kit Stability*:

Unopened kit stability- The manufacturer provided data that supports a real-time stability claim of 12 months.

Open-vial stability- The manufacturer provided data that the RF Reagent, Calibrator and Controls can be stored opened at 2–8°C for up to 3 months.

On-board stability- The manufacturer provided data that the RF Reagent can be stored on-board the Optilite Analyzer for at least 30 days.

d. Detection limit:

The detection limits of the assay were evaluated based on CLSI EP17-A. Study results follow the explanation below:

The Limit of Blank (LoB) was based on 60 determinations of a blank sample

(consisting of a pool of analyte-depleted samples) and was estimated as the 95% percentile of the distribution.

The Limit of Detection (LoD) was calculated according to the equation LoB + 1.645 x SDs where SDs, the standard deviation, was based on six determinations of four samples with analyte levels near the lower limit of the reportable range.

The Limits of Quantitation (LoQ) were calculated from the total error of the LoD study; four separate dilutions of the International Reference Preparation were prepared, and tested three times each on two lots using the test assay on the Optilite analyser over four days. The total error at LoQ was within the maximum allowable total error for each sample matrix. The bottom of the measuring range, 7 IU/mL is set at the limit of quantitation (LoQ) for this assay.

Summary:
LoB = 0.000 IU/mL
LoD = 0.142 IU/mL
LoQ = 7 IU/mL

e. Analytical specificity:

Interferences were assessed according to CLSI EP7-A2 by testing samples at different RF concentrations (8.3, 12.2, 80). Each sample was spiked with interfering substances and tested and compared with results from non-spiked samples. The data demonstrated that the assay was not affected by the following substances at the concentrations given below.

Interferent	**Concentration**	**Interferent**	**Concentration**
Ascorbic Acid	342 µmol/L	Acetylsalicylic	1.815 mmol/L
Conj. Bilirubin	200 mg/L	Penicillin	75 mg/L
Hemoglobin	4 g/L	Caffeine	308 µmol/L
Intralipid	500 mg/dL	Prednisolone	100 µg/mL
Triglyceride	500 mg/dL	Digoxin	7.8 nmol/L
Acetaminophen	1324 µmol/L	Cimetidine	79.2 µmol/L
Ibuprofen	2425 µmol/L	Theophylline	222 µmol/L
Methotrexate	2 mmol	Phenytoin	198 µmol/L

f. Assay cut-off:

Not applicable

2. Comparison studies:

a. Method comparison with predicate device:

A comparison study was performed by testing the predicate and the Optilite RF Kit with 103 samples (including 19 Rheumatoid Arthritis, 1 Osteoarthritis, 1 Psoriatic arthritis, 1 SLE, 3 Sjögrens Syndrome, 3 HCV, 1 Ulcerative Colitis, , 2 Syphylis, 2 Systemic Sclerosis, 1 Vasculitis, and 69 other clinical conditons) all within the assays' measuring ranges; the samples covered the range 8.1–589 IU/mL. The Pearson's correlation coefficient (r value) was 0.984 and the Passing Bablok regression analysis generated the following results:

$$y = 0.90x + 2.51 \text{ IU/mL} \quad (y = \text{Optilite}; x = \text{predicate})$$

(95% CI: Intercept = 0.76–3.88; Slope = 0.87–0.97)

The same comparison study was also analyzed by calculating the % Positive Agreement, % Negative Agreement and % Overall Agreement calculations with the following results:

		Predicate Assay		
		Positive	Negative	Total
Optilite RF Kit	Positive	92	2*	94
	Negative	4**	5	9
	Total	96	7	103

Positive Percent Agreement: 95.8% (92/96) *(95% CI: 95.8% – 98.4%)*
Negative Percent Agreement: 71.4% (5/7) *(95% CI: 35.9% – 91.8%)*
Overall Percent Agreement: 94.2 % (97/103) *(95% CI: 87.8% – 97.3%)*

b. Matrix comparison:

Not applicable; serum is the only sample matrix indicated for this assay.

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):

4. Clinical cut-off**:**

   Not applicable.

5. Expected values/Reference range:

   The expected value of rheumatoid factor in normal serum in the predicate assay is < 12.5 IU/mL. To verify that the predicate's reference range can be used in the Optilite assay, 50 apparently normal U.S. serum samples were tested with a protocol based on CLSI C28-A3. Only one of the 50 samples exceeded 12.5 IU/mL, thus verifying the predicate device's reference interval. The manufacturer encourages users to develop their own laboratory's reference range.

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.