510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY

A. 510(k) Number:
k041891

B. Purpose for Submission:
New device

C. Measurand:
Rheumatoid Factor (RF)

D. Type of Test:
Quantitative, Latex-enhanced nephelometry

E. Applicant:
The Binding Site, Ltd.

F. Proprietary and Established Names:
MININEPH™ Human 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:
   82 Immunology

H. Intended Use:
1. Intended use(s):
   This kit is designed for the *in vitro* measurement of human Rheumatoid Factor in serum using MININEPH™. Measurement of Rheumatoid Factor may aid in the diagnosis of rheumatoid arthritis.

2. Indication(s) for use:
   Same as intended use.

3. Special conditions for use statement(s):
   The device is for prescription use only.

4. Special instrument requirements:
   MININEPH ™ Instrument.

I. Device Description:
The MININEPH™ Human Rheumatoid Factor Kit consists of:
1. Human RF Reagent - aggregated (denatured) human IgG coated onto polystyrene microparticles in lyophilized form.

2. Swipe Card - encoded with details of the reaction curve specific to the respective lot of reagent.

3. RF Buffer.

4. Human RF High and Low Controls - pooled human sera supplied in stabilized liquid form.

All these reagents are to be used on the MININEPH™ Instrument.

J. Substantial Equivalence Information:
1. Predicate device name(s):
   K-ASSAY Rheumatoid Factor

2. Predicate 510(k) number(s):
   k991409

3. Comparison with predicate:

Item	Device	Predicate
	MININEPH™ Human Rheumatoid Factor Kit	**K-ASSAY Rheumatoid Factor**
Similarities		
Indications for Use	As an aid in the diagnosis of rheumatoid arthritis	Same
Sample matrix	Serum	Same
Differences		
Methodology	Latex-enhanced nephelometry	Immunoturbidimetry
Measuring range	31-500 IU/mL	5-320 IU/mL
Calibration	Lot specific magnetic swipe card	Multi-point calibration
Expected results	Less than 19 IU/mL	Less than 10 or 11 IU/mL

K. Standard/Guidance Document Referenced (if applicable):
None referenced.

L. Test Principle:
The determination of soluble antibody concentration by nephelometric methods involves a reaction with the antigen bound to a latex particle to form insoluble complexes. When light is passed through the suspension formed, a portion of the light is scattered and detected by a photodiode. The amount of light scattered is directly 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:*
        Within run Precision:
        These data represent the %CV of ten measurements at three analyte concentrations.

RF (IU/mL)	Mean %CV
247	2.54
121	4.24
19.4	7.19

Between Run Precision
Assays were performed at three different concentrations on 10 separate occasions. The %CV of the 10 results at each concentration was calculated.

RF (IU/mL)	Mean %CV
237	5.81
114	4.34
19.78	4.52

Between Instrument Precision
Assays were performed at three different concentrations on each of five instruments. The %CV of the results at each concentration was calculated.

RF (IU/mL)	Mean %CV
250	6.20
117	5.28
18.55	7.56

     b. *Linearity/assay reportable range:*
        Linearity of this assay at the standard sample dilution of 1/40 was confirmed using a serially diluted serum sample. Regression analysis showed $y = 0.953x + 12.29$ (where y = measured concentration and x = theoretical concentration) over an observed range of 51 IU/mL to 229 IU/mL. The correlation coefficient $r^2 = 0.999$.

Linearity was also performed at a sample dilution of 1/11. Regression equation over the range 20-122 IU/mL was y = 0.9633x + 4.3293, r^2 = 0.9988.

c. *Traceability, Stability, Expected values (controls, calibrators, or methods):*
Calibration materials have been evaluated against the WHO International Preparation of Rheumatoid Arthritis Serum NIBSC 64/2.

The mean calibration curve (encoded in the Minineph swipe card) is acceptable if the internal reference (IR) is within ± 8.5% of the expected value. Three operators assayed each control in triplicate for two days with a total of 18 results. The mean of these 18 results is taken as the assigned value for the control if the CV is < 8.5%.

d. *Detection limit:*
The assay sensitivity limit is 8.6 IU/mL when using 1/11 sample dilution. The sensitivity limit is established based on the measuring range of the curve at the minimum dilution of 1/11. The curve is constructed using the Internal Reference (with target value of 500 IU/mL ±10%). At dilutions of 1/43 to 1/688, the curve range is from 0.73 IU/mL to 11.63 IU/mL. With the standard 1/40 dilution, the range is from 29.2 IU/mL to 465.2 IU/mL and with the minimum 1/11 dilution, the range is 8.03 IU/mL to 127.93 IU/mL. The sensitivity limit of 8.6 IU/mL is selected and is 7.5% higher than lowest value of the range at the 1/11 dilution. The sensitivity limit at the standard 1/40 dilution is 31 IU/mL.

e. *Analytical specificity:*
Interference Study:
Interference was assessed by adding high concentrations of triglycerides (chyle at 16700 units), hemoglobin (100 mg/mL), and bilirubin (8 mg/mL) to an RF control containing a known RF concentration. The percentage interference was calculated from comparison with blanks. All assays were performed in triplicate. The study demonstrates that no interference was observed at the stated concentrations.

Minimal assay interference (< 10%) was demonstrated when pure preparations of IgA, IgM and IgG were added to a sample tested at 1/11 dilution.

f. *Assay cut-off:*
Serum samples were obtained from 120 normal adult blood donors aged 17-70 years and 97.5% of the samples gave results below 19 IU/mL. The mean RF was 8.834 IU/mL with a SD of 2.46 IU/mL.

2. Comparison studies:
   a. *Method comparison with predicate device:*

Correlation study was performed on 42 clinical serum samples using the Minineph™ Human RF kit and the predicate device K-ASSAY Rheumatoid Factor Kit. The 42 samples in the study were from the Clinical Immunology at Queen Elizabeth Hospital, Birmingham, UK. Sex or ages of these patients were not provided. Linear regression analysis showed Minineph RF = 0.9509(K-ASSAY RF) + 0.7918 and correlation coefficient r = 0.9791.

    b. Matrix comparison:
    Serum is the only recommended matrix

3. Clinical studies:
    a. Clinical Sensitivity:
    Not provided.

    b. Clinical specificity:
    Not provided.

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

4. Clinical cut-off:
    See Assay cut-off.

5. Expected values/Reference range:
    The expected value in normal population is less than 19 IU/mL.

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.