

**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY**

A. 510(k) Number:

k081827

B. Purpose for Submission:

New device

C. Measurand:

IgA antibody

D. Type of Test:

Quantitative

E. Applicant:

The Binding Site, Ltd.

F. Proprietary and Established Names:

Human IgA Liquid Reagent Kit for use on SPA_{PLUS}TM

G. Regulatory Information:

1. Regulation section:

21 CFR § 866.5510 Immunoglobulins A, G, M, D, E Immunological Test System

2. Classification:

Class II

3. Product codes:

CFN, Method, Nephelometric, Immunoglobulins (G, A, M)

4. Panel:

Immunology 82

H. Intended Use:

1. Intended use(s):

This kit is intended for the quantitative *in vitro* determination of human IgA in serum, lithium heparin or EDTA plasma, using the Binding Site SPA_{PLUS}TM turbidimetric analyser. Measurement of IgA aids in the diagnosis of abnormal protein metabolism and the body's lack of ability to resist infectious agents. The test results are to be used in conjunction with other clinical and laboratory findings.

2. Indication(s) for use:

Same as intended use.

3. Special conditions for use statement(s):

For prescription use only.

4. Special instrument requirements:

The Binding Site SPA_{plus}TM

I. Device Description:

The device consists of the following: monospecific sheep anti-IgA antisera in liquid form in the presence of preservatives. Calibrators 1-6; Normal and High controls in liquid form; and IgA reaction buffer. The reagents contain 0.099% sodium azide as preservative.

J. Substantial Equivalence Information:

1. Predicate device name(s):

Roche Tina-quant IgA Gen.2/ Hitachi

2. Predicate K number(s):
k040435
3. Comparison with predicate:

Similarities		
Item	Device	Predicate
Detection Method	Turbidimetric immunoassay	Same
Traceability	Standardized against CRM 470 International Reference Material	Same
Controls	Normal and High levels liquid ready to use	Same

Differences		
Item	Device	Predicate
Intended Use	Quantitative determination of IgA in serum or lithium heparin or EDTA plasma, using the Binding Site SPA _{PLUS} TM turbidimetric analyser	Quantitative determination of IgA in serum or lithium/sodium heparin or EDTA plasma, using the Roche automated clinical analysers
Sample Matrix	Human serum; lithium heparin or EDTA plasma	Human serum; lithium/sodium heparin or EDTA plasma
Antibodies	Sheep	Goat
Instruments	SPA _{PLUS} TM analyser	Roche/ Hitachi analyser
Measuring range	0.2 – 7.0 g/L	Hitachi 902: 0.5 – 8 g/L
Reference Range	0.85 – 4.99 g/L	Adults: 0.7 – 4.0 g/L Additional ranges for children

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

CLSI (NCCLS) EP-5A: Evaluation of Precision Performance of Clinical Chemistry.

L. Test Principle:

The determination of soluble antigen concentration by turbidimetric methods involves the reaction with specific antisera 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 within the instrument.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:
 - a. *Precision/Reproducibility:*

The intra-assay precision was determined by testing three serum samples twenty one times. The inter-assay precision was determined by testing three serum samples tested in three times with two runs per day for 21 days. Results are summarized below.

Intra-assay:

Anti-IgA			
n=21	SD	Concentration (g/L)	% CV
Sample 1	0.06	5.895	1.0
Sample 2	0.025	3.606	0.7
Sample 3	0.003	0.340	0.9

Inter-assay:

Anti-IgA			
n=21	SD	Concentration (g/L)	% CV
Sample 1	0.08	5.895	1.4
Sample 2	0.06	3.606	1.7
Sample 3	0.01	0.340	1.0

b. Linearity/assay reportable range:

Linearity across the assay range (0.2-7.0 g/L) was confirmed by testing three sera with normal range concentrations from 5.7-6.7.g/L and two sera with high concentrations from 26.6-27.2 g/L. The samples were serially diluted 9 times with buffer (1:10) down to the lower measuring range (0.2 g/L). All testing were performed twice. The regression plot equations where y is the measured level of IgA concentration and x the theoretical concentration were:
 $y = 1.001x - 0.0585$ (g/L), $r = 0.999$ for IgA

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

An internal reference standard (IR7990) was assigned by comparison with the CRM470 International Reference Material.

Stability: The expiration date claims are 6 months for the IgA unopened Kit; 3 months for the opened IgA kit; and 30 days for on-board IgA kit.

d. Detection limit:

The detection limit was determined by testing a blank sample, the lowest calibrator, and a sample with value close to the blank sample (0.0006g/L) 60 times each. The limit of quantitation for this assay is defined as the lowest point of the calibration curve: 0.19 g/L.

e. Analytical specificity:

Interference by endogenous and other substances: A known IgA serum

samples was tested in triplicate with the following interferents: 4.8g/L hemoglobin, 200 mg/dL bilirubin, 5640 FTU of chyle. No interference by these substances was observed. The package insert states that “turbidimetric assays are not suitable for measurement of highly lipemic or hemolyzed samples, or samples containing high levels of circulating immune complexes due to the unpredictable degree of non-specific scatter these sample types might generate. Unexpected results should be confirmed using alternative assay method”.

Antigen excess effect:

The possibility of antigen excess occurring when using the device on The Binding Site Spa plus™ was evaluated with a serum sample with IgA concentration above the assay range (35 g/L). No antigen excess effect up to 28 g/L of IgA was observed.

f. *Assay cut-off:*

Not provided

2. Comparison studies:

a. *Method comparison with predicate device:*

Testing was performed on 134 sera and 11 plasma samples (29 normal and 116 known elevated and suppressed IgA samples).

The table below shows the comparison of 145 serum and plasma samples ranging from 0.11- 47.7 g/L IgA that were tested with the Binding Site Spa plus™ IgA assay and the predicate device Roche/Hitachi System. Regression analysis of these samples is summarized below:

	n	Slope	Intercept	r
The Binding Site Spa plus™ vs Roche/ Hitachi analyzer	145	0.963	0.086	0.995

b. *Matrix comparison:*

Serum vs. lithium heparin plasma

Thirty three sera and plasma samples, covering the IgA assay measuring range 0.3 – 9.88 g/L for lithium heparin; and twenty four sera and plasma samples, covering the IgA measuring range 0.8 – 4.5g/L for EDTA were compared to determine if any significant bias existed between matrices. The correlation coefficients were acceptable and no bias was observed. Linear regression equations were as follows:

Lithium heparin plasma vs serum:

$$y = 0.919x + 0.127; r = 0.999 (R^2 = 0.998)$$

EDTA plasma vs serum:

$$y = 0.941x + 0.66; r = 0.998 (R^2 = 0.997)$$

3. Clinical studies:
 - a. *Clinical Sensitivity and specificity:*
None provided.
 - b. Other clinical supportive data (when a. is not applicable):
Not applicable.
4. Clinical cut-off:
Not provided
5. Expected values/Reference range:
Adult normal range was assessed on a total 258 normal adult sera samples. 127 normal sera were obtained from healthy adult blood donors (age 17-70 years old) supplied by the UK Blood Transfusion service. A further 131 normal sera samples were from US individuals. The assays were performed on the Binding Site SPA_{plus}TM analyser. A non-parametric distribution of IgA results was seen that gave a 95 percentile reference interval of 0.85-4.99 g/L with a mean of 0.2464 g/L and a median of 2.297 g/L.

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.

