

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

A. 510(k) Number:

k100588

B. Purpose for Submission:

New device

C. Analyte:

Human IgA1 and IgA2

D. Type of Test:

Quantitative, turbidimetric

E. Applicant:

The Binding Site, LTD.

F. Proprietary and Established Names:

Human IgA1 Kit for use on SPAPLUS™

Human IgA2 Kit for use on SPAPLUS™

G. Regulatory Information:

1. Regulation section:

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

3. Classification:

Class II

3. Product code:

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

4. Panel:

Immunology (82)

H. Intended Use:

1. Intended use(s):

For *in vitro* diagnostic use. These kits are intended for quantifying human IgA1 and IgA2 in serum using the Binding Site SPAPLUS turbidimetric analyzer.

2. Indication(s) for use:

Measurement of this immunoglobulin aids in the diagnosis of abnormal protein metabolism and the body's lack of ability to resist infectious agents.

3. Special conditions for use statement(s):

Prescription use only

4. Special instrument requirements:

For use on the SPAPLUS™ analyzer. This instrument is the same analyzer manufactured by Tokyo Boeki Medical Systems, LTD previously cleared and sold under the trade names Prestige, MGC240, and SIRRUS (k040958).

I. Device Description:

Human IgA1 Kit:

1 x 50 tests Human IgA1 Antiserum

1 x Human IgA1 SPAPLUS Calibrator set 1-6 (6 x 1.0 mL)

2 x 1.2 mL Human IgA Subclass SPAPLUS High Control

2 x 1.2 mL Human IgA Subclass SPAPLUS Low Control

1 x 50 tests IgA1 Reaction Buffer SPAPLUS

Human IgA2 Kit:

- 1 x 50 tests Human IgA2 Latex SPAPLUS
- 1 x Human IgA2 SPAPLUS Calibrator set 1-6 (6 x 1.0 mL)
- 2 x 1.2 mL Human IgA Subclass SPAPLUS High Control
- 2 x 1.2 mL Human IgA Subclass SPAPLUS Low Control
- 1 x 50 tests IgA2 Reaction Buffer SPAPLUS

J. Substantial Equivalence Information:

1. Predicate device name:
Human IgA Subclass Liquid Latex Reagent kits (for use on the Behring BN II Analyzer)
2. Predicate 510(k) number:
k981912
3. Comparison with predicate:

Similarities		
Item	Device	Predicate
Intended Use	For quantifying human IgA subclasses 1 and 2 in serum	Same
Indications for Use	Aids in the diagnosis of abnormal protein metabolism and the body's lack of ability to resist infectious agents	Same
Sample type	Human serum	Same
Antibodies	Sheep anti-human IgA1 and IgA2 (latex reagent)	Same
Controls	High and low controls	Same
Traceability	CRM470	Same

Differences		
Item	Device	Predicate
Method	Turbidimetry	Nephelometry
Instrument	Binding Site SPAPLUS analyzer	BN II analyzer
Number of calibrators	6	1
Measuring Range	IgA1: 450-6300 mg/L IgA2: 74-1225 mg/L	IgA1: 375-6000 mg/L IgA2: 63-1000 mg/L

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

- CLSI EP5-A2, Evaluation of Precision Performance of Quantitative Measurements; 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

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:*

Reproducibility testing followed CLSI EP5-A. Three serum samples (low, medium, and high) were assayed in duplicate for 2 runs per day for 21 days (n=84) on SpaPlus analyzers. Results are shown in the table below:

IgA1:

Sample	Mean (mg/L)	Within Run		Total	
		SD	%CV	SD	%CV
1	4,814	78	1.6	200	4.2
2	3,138	55	1.7	184	5.8
3	554	11	2.0	34	6.1

IgA2:

Sample	Mean (mg/L)	Within Run		Total	
		SD	%CV	SD	%CV
1	1,121	31	2.8	77	6.9
2	684	15	2.3	32	4.7
3	79.9	3.4	4.2	7.5	9.4

Lot-to-lot data:

IgA1:

Sample	Mean (mg/L)	Lot-to-lot	
		SD	%CV
1	4,814	77	1.6
2	3,144	65	2.1
3	576	8.2	1.5

IgA2:

Sample	Mean (mg/L)	Lot-to-lot	
		SD	%CV
1	1,121	78	6.9
2	685	29	4.2
3	79.9	2.1	2.6

b. *Linearity/assay reportable range:*

The procedure used to determine linearity was based on CLSI EP6-A. Serum pools containing high levels of either IgA1 or IgA2 were diluted with serum samples containing low levels of analyte to cover the claimed assay range (11 different dilutions). Each dilution was measured in triplicate using three different kit lots and the results were plotted as mean measured versus expected values.

For IgA1, the measuring range for the assay is 450 – 6000 mg/L. For IgA2, the measuring range for the assay is 74 – 1250 mg/L. Measuring ranges are determined using the analyzer’s standard 1/10 dilutions. Regression parameters are summarized in the table:

		Slope	Intercept (mg/L)	R ²
IgA1 assay	Lot 1	1.02	51	0.999
	Lot 2	1.03	61	0.998
	Lot 3	1.02	70	0.999
IgA2 assay	Lot 1	1.01	13	0.999
	Lot 2	1.01	14	0.998
	Lot 3	1.02	1.3	0.998

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

Traceability: IgA1 and IgA2 results are traceable to the CRM470 international reference standard.

Calibrators and Controls: Calibrators and controls consist of pooled human serum and are supplied in stabilized liquid form with preservatives added. Calibrators span the range 38 – 631.4 mg/L for IgA1 and 5.0 to 122.5 mg/L for IgA2. Note that due to the 1/10 dilution in the assay this corresponds approximately to the measuring range of the assays (see above).

Stability: Stability studies demonstrated that the kits were stable for up to 13 months at 2-8°C. The IgA1 antiserum and reaction buffer and the IgA2 latex reagent and reaction buffer were shown to be stable for at least 30 days when stored on-board the instrument.

d. *Detection limit:*

Limit of blank (LoB) and limit of detection (LoD) were determined according to CLSI EP17-A. LoB was estimated by taking the mean absorbance of 60 replicates of the blank plus two standard deviations. The LoD was estimated as the mean value obtained for samples known to have very low levels of IgA1 or IgA2 using the blank as a zero calibrator. The limit of quantitation

(LoQ) was defined as the assigned level of the lowest calibrator based upon measuring neat (undiluted) sample.

	LoB	LoD	LoQ
IgA1 Kit	3.4 mg/L	15.33 mg/L	34.2 mg/L
IgA2 Kit	0.8 mg/L	1.87 mg/L	4.90 mg/L

e. *Analytical specificity:*

The susceptibility of the two assays to interference was assessed by adding high concentrations of bilirubin (200 mg/L), hemoglobin (4.83 mg/L), and chlye (1530 FTUs) to test serum samples containing known concentrations of IgA1 (~250 mg/L) and IgA2 (~19 mg/L). Low sample concentrations of IgA1 and IgA2 were chosen for these studies so that the proportion of interferent is high compared to the analyte concentration, thereby maximizing any interfering effect. Furthermore, as the assay is performed neat (instead of at the 1/10 dilution), the concentration of interferent in the reaction cuvette is maximized. No significant interference was observed under these conditions.

f. *Assay cut-off:*

Not applicable.

2. Comparison studies:

a. *Method comparison with predicate device:*

Studies were performed correlating the results of the human IgA1 and IgA2 kits on the SPAplus analyzer and the predicate device.

For the IgA1 study, 112 sera samples (30 normal and 82 clinical samples) were tested. Passing-Bablok regression analysis of the results yielded linear regression parameters of $y = 0.99x + 12.59$ mg/L (range: 88 mg/L to 5004 mg/L). Standard linear regression yielded $r = 0.980$.

For the IgA2 study, 89 sera samples (27 normal and 62 clinical samples) were used. Passing-Bablok regression analysis of the results yielded linear regression parameters of $y = 0.99x - 1.16$ mg/L (range: 5.443 mg/L to 1145 mg/L). Standard linear regression yielded $r = 0.994$.

b. *Matrix comparison:*

Not applicable

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:

120 normal serum samples were obtained from healthy US adult blood donors.

Samples were stored at -20°C before testing. A non-parametric distribution of IgA1 and IgA2 results were observed:

	Mean	Median	95 th Percentile Reference Interval
IgA1	1866 mg/L	1752 mg/L	761 – 3282 mg/L
IgA2	393 mg/L	322 mg/L	68.9 - 1143 mg/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.