

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

A. 510(k) Number:

k092450

B. Purpose for Submission:

New device

C. Measurand:

IgD antibody

D. Type of Test:

Quantitative nephelometry

E. Applicant:

The Binding Site, Ltd.

F. Proprietary and Established Names:

Human IgD 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:

CZJ, IgD, Antigen, antiserum, control

4. Panel:

Immunology 82

H. Intended Use:

1. Intended use(s):

This kit is intended for measuring human immunoglobulin D (IgD) in serum as an aid 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-IgD antiserum coated polystyrene latex in liquid with preservatives; Calibrators 1-6; Low and High controls in liquid form; and IgD reaction buffer. The reagents contain 0.099% sodium azide, 0.1% EACA, and 0.01% benzamidine as preservatives.

J. Substantial Equivalence Information:

1. Predicate device name(s):

Binding Site Human IgD Liquid Reagent Kits for use on the Behring BNII Analyser

2. Predicate K number(s):

k051299

3. Comparison with predicate:

Similarities		
Item	Device	Predicate
	Human IgD Kit for use on SPA _{PLUS} TM	Human IgD Liquid Reagent Kits for use on the Behring BNII Analyser
Intended Use	Quantitative determination of IgD in serum	Same
Detection Method	Nephelometric immunoassay	Same
Traceability	Standardized against Human Serum Immunoglobulin D NIBSC 67/037 British Reference Standard	Same
Controls	Low and High levels liquid ready to use	Same
Sample Matrix	Human serum	Same
Antibodies	Sheep Anti-Human IgD	Same

Differences		
Item	Device	Predicate
	Human IgD Kit for use on SPA _{PLUS} TM	Human IgD Liquid Reagent Kits for use on the Behring BNII Analyser
Instruments	SPA _{PLUS} TM analyser	BN TM II analyser
Measuring range	7.0 - 210 mg/L at 1:10 dilution 140-4400 mg/L at 1:10 dilution 560 -17600 mg/L at 1:40 dilution (extended dilution with 1:20 off line)	6.5 – 207.5 mg/L at 1:100 dilution 130 – 4150 mg/L at 1: 2000 dilution
Reference Range	7.7 – 132.1 mg/L	1.3 – 152.7 mg/L

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

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

CLSI (NCCLS) EP-17A: Protocols for Determination of LOD and LOQ

CLSI (NCCLS) EP-6A: Evaluation of Linearity of Quantitative Measurements

L. Test Principle:

The determination of soluble antigen concentration by nephelometric 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 photoiodide 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 three times per run and two runs per day for 21 days. Results are summarized below.

Intra-assay:

Anti-IgD			
n=21	SD (mg/L)	Mean Concentration (mg/L)	% CV
Sample 1	2.50	169.42	1.5
Sample 2	1.44	122.60	1.2
Sample 3	0.26	11.66	2.3

Inter-assay:

Anti-IgD			
n=21	SD (mg/L)	Mean Concentration (mg/L)	% CV
Sample 1	1.86	169.42	1.1
Sample 2	1.44	122.60	0.9
Sample 3	0.25	11.66	2.2

b. *Linearity/assay reportable range:*

Linearity across the assay measuring range (7.0 - 210 mg/L) was confirmed by testing two pooled sera with low range concentrations from 25 – 27 mg/L and two pooled sera with high concentrations from 89-97 mg/L. The samples were serially diluted 1:10 with buffer 11 times to the lower measuring range (7.0 mg/L). The diluted samples were re-assayed on three different lots of IgD kits. The regression equations on the three IgD lots where y is the measured level of IgD concentration and x the theoretical concentration were as follows:

$$y = 0.9972x - 2.76, R^2 = 0.9983;$$

$$y = 1.0223x - 0.8784, R^2 = 0.9992; \text{ and}$$

$$y = 0.9988x - 4.7, R^2 = 1.0.$$

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

The calibrators are traceable to the Human Serum Immunoglobulin D NIBSC 67/037 British Reference Standard.

Stability: The expiration date claims are 13 months for the IgD unopened kit and 28 days for on-board IgD 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 (0.6 mg/L) 60 times each. The limit of quantification for this assay is defined as the lowest

point of the calibration curve: 6.33 mg/L.

e. Analytical specificity:

Interference by endogenous and other substances: A serum sample with known IgD concentration was tested in triplicate with the following interferents: 4.8 mg/L hemoglobin, 200 mg/dL bilirubin and 1560 FTU of chyle. No significant interference by these substances was observed. The package insert states that “microbial contaminated, lipemic, hemolyzed or samples containing particulate matter should not be used”.

Antigen excess effect:

No antigen excess effect up to 1680 mg/L of IgD was observed.

f. Assay cut-off:

The assay cut-off was determined to be the upper limit of 120 sera from normal healthy adults in the United Kingdom and was 132.1 mg/L. To validate the cut-off, fifteen IgD myeloma samples were tested and all had IgD concentrations >132.1 mg/L.

2. Comparison studies:

a. Method comparison with predicate device:

Testing was performed on 97 sera samples (50 normal and 47 clinical samples) with the new device “The Binding Site Human IgD kit for use on Spa plus™” and the predicate device “The Binding Site Human IgD Liquid reagent Kit for use on the Behring BN™ II analyser”. The IgD concentration ranged from 7.7- 51,352 mg/L. Forty six of the 50 normal samples had normal IgD levels and 4 had elevated IgD. Seventeen of the 47 clinical samples were from IgD myeloma clinic and had elevated IgD. Thirty of the 47 clinical samples were from general clinic and all 30 had normal IgD levels.

The regression analysis of the comparison study is summarized below:

	n	Slope	95% CI	Intercept	95% CI	r
The Binding Site Spa plus™ vs BN™ II analyser	97	0.950	0.91 – 1.01	- 0.590	1.62 – 0.42	0.995

Positive, negative and overall percent agreements between the two devices were 100% (see table below):

		BN™ II analyser		
		Elevated (>152.7 mg/L)	Normal (<152.7 mg/L)	Total
The Binding Site Spa plus™	Elevated (>132.1 mg/L)	21	0	21
	Normal (<132.1 mg/L)	0	76	76
	Total	21	76	97

