510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION MEMORANDUM
ASSAY ONLY TEMPLATE

A. 510(k) Number:

K151759

B. Purpose for Submission:

New monitoring claim

C. Measurand:

Immunoglobulin IgA Kappa (combined α heavy and κ light chain) and Immunoglobulin IgA Lambda (combined α heavy and λ light chain)

D. Type of Test:

Quantitative, Turbidimetry

E. Applicant:

The Binding Site Group, Ltd.

F. Proprietary and Established Names:

Hevylite® Human IgA Kappa Kit for use on the SPAPLUS and Hevylite® Human IgA Lambda Kit for use on the SPAPLUS

G. Regulatory Information:

1. Regulation section:

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

2. Classification:

   Class II

3. Product code:

   OPX - IgA Kappa (Heavy and Light chain Combined). Antigen, antiserum, control
   OPY - IgA Lambda (Heavy and Light chain Combined). Antigen, antiserum, control

4. Panel:

   Immunology (82)

H. Intended Use:

1. Intended use(s):

   Hevylite Human IgA Kappa is a quantitative in vitro assay performed on the Binding Site SPAPLUS for the measurement of IgA Kappa (IgA heavy chain and Kappa light chain intact immunoglobulin) in serum. Measurement of Hevylite Human IgA Kappa is used alongside Hevylite Human IgA Lambda to calculate the IgA Kappa/IgA Lambda ratio. The Hevylite Human IgA Kappa/IgA Lambda ratio can be used when monitoring previously diagnosed IgA multiple myeloma and is used in conjunction with other laboratory tests and clinical evaluations. The assignment of complete response is reliant upon other tests including immunofixation, bone marrow and urine assessments.

   Hevylite Human IgA Lambda is a quantitative in vitro assay performed on the Binding Site SPAPLUS for the measurement of IgA Lambda (IgA heavy chain and Lambda light chain intact immunoglobulin) in serum. Measurement of Hevylite Human IgA Lambda is used alongside Hevylite Human IgA Kappa to calculate the IgA Kappa/IgA Lambda ratio. The Hevylite Human IgA Kappa/IgA Lambda ratio can be used when monitoring previously diagnosed IgA multiple myeloma and is used in conjunction with other laboratory tests and clinical evaluations. The assignment of complete response is reliant upon other tests including immunofixation, bone marrow and urine assessments.

2. Indication(s) for use:

   Same as intended use.

3. Special conditions for use statement(s):

   For prescription use only.

   Warning: The result of Hevylite Human IgA Kappa in a given specimen determined with assays with different manufacturers and different instrument platforms can vary due to differences in assay methods and reagent specificity. The results reported by the laboratory to the physician must include the identity of the Hevylite Human IgA Kappa assay used. Values obtained with different assay methods cannot be used interchangeably. If, in the course of monitoring a patient, the assay method used for determining Hevylite IgA Kappa levels serially is changed, additional sequential testing should be carried out. Prior to changing assays, the laboratory MUST confirm baseline values for patients being serially monitored.

   Warning: The result of Hevylite Human IgA Lambda in a given specimen determined with assays with different manufacturers and different instrument platforms can vary due to differences in assay methods and reagent specificity. The results reported by the laboratory to the physician must include the identity of the Hevylite Human IgA Lambda assay used. Values obtained with different assay methods cannot be used interchangeably. If, in the course of monitoring a patient, the assay method used for

determining Hevylite Human IgA Lambda levels serially is changed, additional sequential testing should be carried out. Prior to changing assays, the laboratory MUST confirm baseline values for patients being serially monitored.

4. Special instrument requirements:

   The Binding Site SPAPLUS Analyzer

I. Device Description:

The Hevylite Human IgA Kappa Antiserum SPAPLUS and Hevylite Human IgA Lambda Antiserum SPAPLUS contain vials of ready-to-use polyclonal monospecific sheep anti-IgA antisera against combined α heavy and κ light chain or combined α heavy and λ light chain, calibrators (six levels), controls (low and high) and reaction buffer in liquid form. The reagents contain 0.099% sodium azide as preservative.

J. Substantial Equivalence Information:

1. Predicate device names and predicate 510(k) number:

   Hevylite™ Human IgA Kappa Kit and Hevylite™ Human IgA Lambda Kit for use on Siemens BN™ II Systems (k140105)

2. Comparison with predicate:

Similarities		
Item	Device Hevylite® IgA Kappa (IgAK) and IgA Lambda (IgAL) Kits on SPAPLUS	Predicate Hevylite™ IgA Kappa (IgAK) and IgA Lambda (IgAL) Kits on Siemens BN™ II
Intended Use	Quantitative in vitro assay for the measurement of IgA Kappa (IgA heavy chain and Kappa light chain intact immunoglobulin) and IgA Lambda (IgA heavy chain and Lambda light chain intact immunoglobulin) in serum. Measurement of Hevylite Human IgA Kappa is used alongside Hevylite Human IgA Lambda to calculate the IgA Kappa/IgA Lambda ratio. The Hevylite Human IgA kappa/IgA lambda ratio can be used when monitoring previously diagnosed IgA multiple	Same

Similarities		
Item	Device Hevylite® IgA Kappa (IgAK) and IgA Lambda (IgAL) Kits on SPAPLUS	Predicate Hevylite™ IgA Kappa (IgAK) and IgA Lambda (IgAL) Kits on Siemens BN™ II
	myeloma and is used in conjunction with other laboratory tests and clinical evaluations. The assignment of complete response is reliant upon other tests including immunofixation, bone marrow and urine assessments.	
Method	Nephelometric/ Turbidimetric	Same
Analyte	IgA Kappa and IgA Lambda	Same
Antibody	Polyclonal monospecific Sheep anti-human combined α heavy and κ light chain or combined α heavy and λ light chain	Same
Control	Binding Site High and Low Control	Same
Sample Matrix	Serum	Same
Capture antibody	Sheep anti-human IgA combined	Same

Differences		
Item	Device Hevylite® IgA Kappa (IgAK) and IgA Lambda (IgAL) Kits on SPAPLUS	Predicate Hevylite™ IgA Kappa (IgAK) and IgA Lambda (IgAL) Kits on Siemens BN™ II
Instrument	Binding Site SPAPLUS	Siemens BN™ II Systems
Measuring Range	At standard 1/10 dilution: IgAK: 0.18 – 11.2 g/L IgAL: 0.16 – 10.4 g/L Extended Range for IgAK: 1/1 dilution: 0.018 – 1.12 g/L 1/60 dilution: 1.08 – 67.2 g/L 1/150 dilution: 2.7 – 168 g/L Extended Range for IgAL: 1/1 dilution: 0.016 – 1.04 g/L 1/60 dilution: 0.96 – 62.4 g/L 1/150 dilution: 2.4 – 156 g/L	At standard 1/100 dilution: IgAK: 0.35 – 11.2 g/L IgAL: 0.33 – 10.4 g/L Extended Range for IgAK: 1/5 dilution: 0.018 – 0.56 g/L 1/20 dilution: 0.07 – 2.24 g/L 1/400 dilution: 1.40 – 44.8 g/L 1/2000 dilution: 7.0 – 224 g/L Extended Range for IgAL: 1/5 dilution: 0.016 – 0.520 g/L 1/20 dilution: 0.065 – 2.08 g/L 1/400 dilution: 1.40 – 41.6 g/L 1/2000 dilution: 6.5 – 208 g/L
Calibrator	Six Level Binding Site	Single level Binding Site Hevylite

Differences		
Item	Device Hevylite® IgA Kappa (IgAK) and IgA Lambda (IgAL) Kits on SPAPLUS	Predicate Hevylite™ IgA Kappa (IgAK) and IgA Lambda (IgAL) Kits on Siemens BN™ II
	Hevylite Calibrator	Calibrator autodiluted by BN II to six different concentrations
Reference Interval	IgAK: 0.65 – 3.10 g/L IgAL: 0.45 – 2.13 g/L IgAK/IgAL Ratio: 0.95 – 2.21	IgAK: 0.48 – 2.82 g/L IgAL: 0.36 – 1.98 g/L IgAK/IgAL Ratio: 0.80 – 2.04

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

CLSI EP05-A2: Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline – Second Edition
CLSI EP06-A: Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach
CLSI EP07-A2: Interference Testing in Clinical Chemistry
CLSI EP17-A: Protocols for Determination of Limits of Detection and Limits of Quantitation
CLSI C28-A3: Defining, Establishing and Verifying Reference Intervals in the Clinical Laboratory

L. Test Principle:

Evaluating the concentration of a soluble antigen (e.g. IgAκ or IgAλ) by turbidimetry involves the addition of the test sample to a solution containing the appropriate antibody (anti-IgAκ or anti-IgAλ) in a reaction vessel or cuvette. A beam of light is passed through the cuvette and, as the antigen-antibody reaction proceeds, the light passing through the cuvette is scattered increasingly as insoluble immune complexes are formed. Light scatter is monitored by measuring the decrease in intensity of the incident beam of light. The antibody in the cuvette is in excess so the amount of immune complex formed is proportional to the antigen concentration. A series of calibrators of known antigen concentration are assayed initially to produce a calibration curve of measured light scatter versus antigen concentration. Samples of unknown antigen concentration can then be assayed and the results read from the calibration curve.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

The within-run, between-run, between-day, between-lot and between-instrument precision were determined by testing three serum samples over 21 days with two runs

per day on three different reagent lots on one analyser. Results are summarized below.

IgAκ Precision studies:

Sample	Mean	Within Run		Between Run		Between Day		Between instrument		Total	
		SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
1	0.360	0.01	3.4	0.00	2.0	0.02	4.8	0.02	4.5	0.02	6.2
2	1.693	0.06	3.5	0.02	1.0	0.07	3.9	0.06	3.4	0.09	5.4
3	2.700	0.04	1.6	0.02	0.8	0.07	2.7	0.05	1.9	0.09	3.2
4	9.508	0.22	2.3	0.00	0.0	0.15	1.6	0.12	1.3	0.27	2.8
5	12.897	0.43	3.4	0.23	1.8	0.27	2.1	0.19	1.4	0.56	4.3

IgAλ Precision studies:

Sample	Mean	Within Run		Between Run		Between Day		Between instrument		Total	
		SD	%C	SD	%CV	SD	%CV	SD	%CV	SD	%CV
1	8.31	0.12	1.4	0.19	2.3	0.05	6.0	0.4	4.7	0.55	6.6
2	1.99	0.04	2.1	0.05	2.4	0.11	5.7	0.09	4.3	0.13	6.5
3	0.26	0.01	3.2	0.01	2.2	0.02	6.9	0.02	5.6	0.02	8.0

b. Linearity/assay reportable range:

A linearity study was performed following CLSI document Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach. The linearity of the IgAK and IgAL assays have been confirmed using serially diluted serum samples to cover the standard measuring range 0.18 – 11.2 g/L and 0.16 – 10.4 g/L respectively. The results demonstrated that the IgAK and IgAL assays are linear over the ranges of 0.1138 – 13.126 g/L and 0.09 – 11.75 with deviation from linearity ≤ 10%.

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

Traceability: An Internal Reference material (IR) was assigned by comparison with the Reference Material DA470K.

A real-time stability study of unopened kits was performed on three lots of IgA Kappa and IgA Lambda SPAPLUS kits with testing time intervals at day 0, 1, 3, 7, 10, 13, 19 months. Data support a shelf life claim of 19 months at 2–8° C.

Open-vial stability was performed on three lots of IgA Kappa and IgA Lambda SPAPLUS kits with testing time intervals at day 0, and 1, 2, and 3 months. Data support the open vial stability claim of 3 months at 2–8° C.

On-board stability was performed on three lots of IgA Kappa and IgA Lambda SPAPLUS kits with testing time intervals at 0, 7, 14, 21, and 35 days. Data support the on-board stability claim of 28 days at 8–12^{o} C, provided that the power is left switched on as stated in the product insert.

All stability results were within the sponsor's acceptance criteria.

d. Detection limit:

The analytical sensitivity was determined in accordance with CLSI EP17-A. The Limit of Blank (LoB) was based on 60 determinations of analyte depleted sample (and was estimated at 95% percentile of the distribution. The Limit of Detection (LoD) was calculated from the LoB and the combined SD of the 5 LoQ samples. The LoQ were calculated from 5 independent samples (from serum samples diluted with analyte depleted serum to achieve a concentration close to the bottom of the measuring range) tested twelve times over five days and the total error (0.0.057 g/L for IgAK and 0.044 g/L for IgAL) were within the maximum allowable total error. The tabulated summary is shown below:

	LoB	**LoD**	**LoQ**
IgA Kappa	0.00 g/L	0.0026 g/L	0.018 g/L
IgA Lambda	0.00 g/L	0.0014 g/L	0.016 g/ L

e. Analytical specificity:

Interference:
Interferences were assessed according to CLSI EP7-A2 by testing five serum samples with different IgA Kappa and IgA Lambda concentration ranges in g/L: (1) normal serum samples, IgAK target levels 1.015 - 1.059 and IgAL target levels 1.151 - 1.140; (2) low concentration serum samples, target levels 0.3000 – 0.414 and 0.311 – 0.325 respectively; (3) high serum samples, target levels 5.984 – 6.162 and 4.093 – 4.600; (4) samples close to the close to the medical decision point (MDP) at the lower limit of the reference range, target 0.585 – 0.603 and 0.414 – 0.435 g/L respectively; (5) high concentration serum samples, target level 1.949 – 2.049 and 2.099 – 2.118 respectively. Each sample was spiked with interfering substances and tested in replicate. The manufacturer's acceptance criteria were that the mean results from the spiked samples must be within ±10% of the mean of the control samples.

No significant assay interference effects were observed when the five samples of IgAK and IgAL were tested with bilirubin at 200mg/L, hemoglobin at 5g/L, triglyceride at 1000mg/dL or Intralipid at 200 mg/dL and the 15 commonly used drugs at the concentrations given below.

Drug	Concentration tested
Acetaminophen	1324 µmol/L
Acetylsalicylic Acid	3.63 mmol/L
Ascorbic Acid	342 µmol/L
Bortezomib	6 mg/mL
Caffeine	308 µmol/L
Cimitidine	79.2 µmol/mL
Cyclophosphamide Monohydrate	60 µg/L
Digoxin	7.8 nmol/L
Ibuprofen	2425 µmol/L
Methotrexate	2 mmol
Penicillin	75 mg/L
Phenytoin	198 µmol/L
Prednisolone	100 µg/mL
Pomalidomide	100 µg/mL
Theophylline	222 µmol/L

Cross reactivity studies:

The study is to assess the possible cross reaction from a series of panel samples of various subtypes. The 76 panel samples analyzed, included 14 IgAκ, 10 IgAλ, 10 IgGκ, 13 IgGλ , 8 IgMκ, 5 IgMλ, 2 Free Kappa, 5 Free Lambda Myeloma samples.

Crossreactivity was assessed by the comparison of total IgA with results obtained from the Hevylite Human IgA Kappa and IgA Lambda Kit testing. No significant crossreactivity was seen with these monoclonal samples.

Antigen Excess Detection

The possibility of antigen excess occurring when using the device on The Binding Site SPAPLUS was evaluated with 13 monoclonal IgA Kappa and 9 monoclonal IgA Lambda samples with concentrations above the 0.18-11.2 g/L and 0.16-10.4g/L standard measuring ranges respectively. No antigen excess effect up to 63.6 g/L of IgAκ and 74.4 g/L of IgAλ concentration levels were observed at 1/1 dilution.

f. Assay cut-off:

Refer to Expected values

2. Comparison studies:

a. Method comparison with predicate device:

IgA Kappa:
A comparison study was performed by analysing 176 serum samples (including 68

IgA Kappa paraprotein and 52 IgA Lambda paraprotein samples, 37 donor samples and 19 other samples, covering the range of 0.02 – 84.8g/L for IgA Kappa and 0.018–54.6 g/L for IgA Lambda) using the Hevylite Human IgA Kappa and IgA Lambda Kit for use on SPAPLUS and an alternative commercially available assay. Passing Bablok regression analysis generated the following results:

y = 1.12x -0.01 g/L (y=SPAPLUS; x=predicate analyzer)

correlation coefficient r= 0.991 (calculated linear regression)

IgA Lambda:

A comparison study was performed by analysing 174 serum samples (including 64 IgA Kappa paraprotein and 54 IgA Lambda paraprotein samples, 37 donor samples and 19 other samples, covering the range of 0.018 – 54.6g/L) using the Hevylite Human IgA Lambda Kit for use on SPAPLUS and an alternative commercially available assay. Passing Bablok regression analysis generated the following results

y = 1.09x - 0.05 g/L (y= SPAPLUS; x=predicate analyzer)

correlation coefficient r = 0.981 (calculated linear regression)

To examine the monitoring claim of the assay and to mimic the previously submitted 449 clinical samples being run on the SPAPLUS, the following regression equation based on the study above was used to transform the data:

	Slope	Intercept
IgA Kappa	1.12	-0.01
IgA Lambda	1.09	-0.05

The slope and the intercept were applied using the following equation: (*Original result* × *Slope*) + *Intercept*

As the intercepts were negative, data that were already close to LoQ were transformed into negative values. Negative IgA Kappa and IgA Lambda results are not possible. Results that were transformed were capped at LoQ (IgA Kappa: 0.018g/L and IgA Lambda: 0.016g/L). 3000 bootstrapped patient data points were compared and Passing Bablok regression equations were generated with the following results:

Assay	N	Sample Range (on predicate)	Regression Equation	Slope 95% CIs	Intercept 95% CIs
IgA Kappa	2718	0.02 to 84.8g/L	Y=1.119x – 0.008	1.113 to 1.125	-0.02 to 0.001
IgA Lambda	2770	0.018 to 54.6g/L	Y= 1.096x – 0.055	1.085 to 1.109	-0.06 to -0.05
IgA Kappa / IgA Lambda	2480	0.001 to 655.22	Y= 1.208x – 0.05	1.175 to 1.240	-0.07 to -0.02

b. Matrix comparison:

Not applicable

3. Clinical studies:

a. Clinical Sensitivity/ clinical specificity:

Purpose of the study

The purpose of this study was to compare the clinical monitoring performance of the predicate and the SPA_{PLUS} Hevylite Human IgA Kappa and IgA Lambda Kit results obtained from samples taken at multiple time points from IgA Kappa and IgA Lambda multiple myeloma patients during the course of their disease to assess clinical performance. TBS has generated Passing and Bablok regression equations for the comparison study of the SPA_{PLUS} kits against the predicate kits. The regression equation modelling would then be applied to the existing BNII 449 monitoring sample results.

Table 1: HLC Monitoring Response Category

Complete Response (CR)	HLC ratio within the normal range, negative urine immunofixation (where available) and ≤5% plasma cells in bone marrow.
Very Good Partial Response (VGPR)	>94% reduction of HLC ratio from baseline and urine M-immunoglobulin level <100mg/24hrs.
Partial Response (PR)	Reduction of HLC ratio from baseline between 60 – 94% and reduction in 24hr urinary M-immunoglobulin by ≥90% from baseline or ≤200mg/24hrs.
Stable Disease (SD)	A change in HLC ratio from baseline <24% increase but <60% reduction
Progressive Disease (PD)	≥24% increase in HLC ratio from baseline (the absolute increase in involved IgA must be ≥5g/L) or ≥25% increase in urine M-immunoglobulin from baseline (the absolute increase must be ≥200mg/24hrs).

Pivotal Study

A pivotal study was conducted on patient samples over multiple time points on both test device and predicate devices. Assignment of classification was based on the HLC Monitoring Response Category detailed in Table 1, using all assay data available. Responses were categorized in accordance with NCCN Guidelines v.1.2011 by using the percentage (%) change in SPEP or total IgA from baseline. Responses were characterized as progressive disease (PD), stable disease (SD), partial response (PR), very good partial response (VGPR) and complete response (CR). Kappa Statistics was used to evaluate the agreement between test and predicate devices.

Study Design

A comparison study of 35 monitoring samples from 12 IgA Kappa patients and 10 IgA Lambda patients was performed. Every sample was analysed in singlicate on

both the IgA Kappa and IgA Lambda kits on the predicate (BNII) and the SPA$_{PLUS}$ assays. Each patient was then analysed individually, comparing the results obtained on the predicate and the SPA$_{PLUS}$ assays.

		K140105 HLC Response					**Total**
Observed		**CR**	**VGPR**	**PR**	**SD**	**PD**	
SPA$_{PLUS}$ HLC Response	CR	0	0	0	0	0	**0**
	VGPR	0	4	0	0	0	**4**
	PR	0	0	2	0	0	**2**
	SD	0	0	1	27	0	**28**
	PD	0	0	0	0	1	**1**
Total		**0**	**4**	**3**	**27**	**1**	**35**
Kappa (95% CIs)		1.00 (1.00 to 1.00)					
Weighted Kappa (95% CIs)		0.95 (0.85 to 1.05)					

Data Modeling

Data modeling procedure was carried out in the remaining patient samples which were not being included in the pivotal study. The Passing and Bablok regression equations derived from the method comparison study of the SPA$_{PLUS}$ kits against the predicate kits were applied to the existing BNII results and simulate the 449 samples used in the clinical study being run on the SPA$_{PLUS}$ kits. The statistical regression equation modelling results are summarized in the Table below.

Observed		**Predicate HLC response**					
		CR	**VGPR**	**PR**	**SD**	**PD**	**Total**
Regression Equation Modelling	CR	25	0	0	0	0	**25**
	VGPR	3	145	8	0	0	**156**
	PR	0	10	113	9	0	**132**
	SD	0	0	1	114	2	**117**
	PD	0	0	0	0	19	**19**
	Total	**28**	**155**	**122**	**123**	**21**	**449**
Kappa (95% CIs)		0.90 (0.88 to 0.92)					
Linear Weighted Kappa (95% CIs)		0.93 (0.92 to 0.95)					
Quadratic Weighted Kappa (95%CIs)		0.99 (0.98 to 0.98)					

The HLC SPA_{PLUS} IgA Monitoring Response Category in Table 1 above was derived from the NCCN v1.2011 *Guidelines on Treatment Response Classification* as shown in Table 2:

Table 2: Comparison of Treatment Response Classification – NCCN v1.2011 and Hevylite IgA kappa/lambda ratio (HLC ratio)

Response	NCCN v1.2011	Disease Monitoring Using HLC SPA_{PLUS} IgA
Complete Response (CR)	**Negative IFE** on the serum and urine and disappearance of any soft tissue plasmacytomas and ≤5% plasma cells in bone marrow	**HLC ratio** within the **norma**l range (SPA_{PLUS} IgAκ/IgAλ Ratio 0.95-2.21) and negative urine immunofixation and ≤5% plasma cells in bone marrow (where available)
Very Good Partial Response (VGPR)	Serum and urine **M protein detectable by IFE but not SPEP** or ≥90% reduction in serum M protein level plus urine M protein level <100 mg per 24 hours	**>94% reduction of HLC ratio from baseline** and urine M protein level <100 mg per 24 hours.
Partial Response (PR)	**≥50% reduction of serum M protein** and reduction in 24 hour urinary M protein by ≥90% or to <200 mg per 24 hours.	**Reduction of HLC ratio from baseline between 60 – 94%** and reduction in 24 hour urinary M protein by ≥90% or to <200 mg per 24 hours.
Stable Disease (SD)	Not meeting criteria for CR, VGPR, PR or progressive disease	A change in HLC ratio from baseline **<24% increase but <60% reduction.**
Progressive Disease (PD)	**Increase of ≥25%** from baseline in 1 or more: • Serum M-component and/or (the absolute increase must be ≥0.5 g/dL) • Urine M component and/or (the absolute increase must be ≥200mg/24hr) • Bone marrow plasma cell percentage: the absolute percentage must be ≥10%	**≥24% increase in HLC ratio** from baseline (the absolute increase in involved IgA must be ≥ 5 g/L) or a ≥25% increase in urine M-component from baseline (the absolute increase must be ≥200mg/24hr)

Response	NCCN v1.2011	Disease Monitoring Using HLC SPA_{PLUS} IgA
	• Definite development of new bone lesions or soft tissue plasmacytomas or definite increase in the size of existing bone lesions or soft tissue plasmacytomas • Development of hypercalcemia	

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

Not applicable

4. Clinical cut-off**:**

Refer to discussion above.

5. Expected values/Reference range:

Reference Adult Serum	Mean	Median	95 Percentile Range
IgA Kappa (g/L)	1.53	1.42	0.65 – 3.10
IgA Lambda (g/L)	1.06	0.95	0.45 – 2.13
IgA Kappa/ IgA Lambda Ratio	1.48	1.45	0.95 – 2.21

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.