



Food and Drug Administration  
10903 New Hampshire Avenue  
Document Control Center – WO66-G609  
Silver Spring, MD 20993-0002

August 25, 2016

The Binding Site Ltd.  
Mr. Jon Lauder  
Regulatory Affairs Officer  
8 Calthorpe Road, Edgbaston,  
Birmingham, West Midlands, B15 1QT  
UK

Re: K153560

Trade/Device Name: Optilite® Low Level Albumin Kit  
Regulation Number: 21 CFR 866.5040  
Regulation Name: Albumin immunological test system  
Regulatory Class: Class II  
Product Code: DCF  
Dated: July 22, 2016  
Received: July 26, 2016

Dear Mr. Lauder:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); medical device reporting (reporting of

medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801), please contact the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address

<http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm>. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to

<http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm> for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address

<http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm>.

Sincerely,

**Kelly Oliner -S**

For

Leonthena Carrington, MBA, MS, MT(ASCP)

Director

Division of Immunology and Hematology Devices

Office of In Vitro Diagnostics

and Radiological Health

Center for Devices and Radiological Health

Enclosure

## Indications for Use

510(k) Number (if known)

Device Name

Optilite Low Level Albumin Kit

Indications for Use (Describe)

The Optilite Low Level Albumin Kit is intended for the quantitative in vitro measurement of albumin in CSF, urine and serum using the Binding Site Optilite analyser to aid in the diagnosis of kidney and intestinal diseases. This test should be used in conjunction with other laboratory and clinical findings.

Type of Use (Select one or both, as applicable)

☒ Prescription Use (Part 21 CFR 801 Subpart D)

☐ Over-The-Counter Use (21 CFR 801 Subpart C)

### CONTINUE ON A SEPARATE PAGE IF NEEDED.

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<b>Optilite Low Level Albumin Kit</b>
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**510(k) SUMMARY**

**A. 510(k) Number:**

K153560

**B. Purpose for Submission:**

New device

**C. Measurand:**

Albumin

**D. Type of Test:**

Quantitative immunoturbidimetry

**E. Applicant:**

The Binding Site

**F. Proprietary and Established Names:**

Optilite<sup>®</sup> Low Level Albumin Kit

**G. Regulatory Information:**

1. Regulation section:

21 CFR 866.5040, Albumin immunological test system

2. Classification:

Class II

3. Product code:

DCF – Albumin antigen, antiserum, control

4. Panel:

Immunology (82)

## H. Intended use:

### 1. Intended use(s):

The Optilite Low Level Albumin Kit is intended for the quantitative in vitro measurement of albumin in CSF, urine and serum using the Binding Site Optilite analyser to aid in the diagnosis of kidney and intestinal diseases. This test should be used in conjunction with other laboratory and clinical findings.

### 2. Indication(s) for use:

Same as Intended use.

### 3. Special conditions for use statement(s):

Prescription use only

### 4. Special instrument requirements:

Optilite Analyser (Indiko) (K110035)

## I. Device Description:

The Optilite Low Level Albumin Kit is comprised of the following reagents:

Antiserum: Supplied in stabilised liquid form. Preservatives: 0.099% sodium azide, 0.1% E-amino-n-caproic acid (EACA), 1mM ethylenediamine-tetraacetic acid (EDTA) and 0.01% benzamidine..

Calibrator and Controls: Pooled human serum, supplied in stabilised liquid form. Containing 0.099% sodium azide, 0.1% EACA and 0.01% benzamidine as preservatives. The concentration given on the quality control certificate has been obtained by comparison with the DA470k international reference material.

Reaction Buffer: Containing 0.099% sodium azide as a preservative.

Note - In Optilite kits, the antiserum reagent and reaction buffer are supplied in a single wedge with a chamber for each fluid. They are therefore labelled as a single component *Optilite LLAlb Reagent*. The Antigen Excess Control does not have an assigned value.

## J. Substantial equivalence information:

### 1. Predicate device name(s) and 510(k) number(s):

N Antiserum to Human Albumin K972929  
N Protein Standard SL K964062  
NT Protein Control SL K964065

2. Comparison with predicate:

Similarities		
Item	Test device	Predicate
Assay type	Quantitative	same
Adult Reference Interval	Serum: 35000 - 52000mg/L Urine: <30mg/L CSF: <350mg/L	same
Specimen Type	Serum, Urine, CSF	Same (also heparinized and EDTA plasma)
Intended use	The Optilite Low Level Albumin Kit is intended for the quantitative in vitro measurement of albumin in CSF, urine and serum using the Binding Site Optilite analyser to aid in the diagnosis of kidney and intestinal diseases. This test should be used in conjunction with other laboratory and clinical findings.	In-vitro diagnostic reagent for the quantitative determination of albumin in human serum, heparinized and EDTA plasma, as well as in human urine and cerebrospinal fluid (CSF) by means of immunonephelometry on the BN Systems.
Calibration	ERM®-DA470k/IFCC	same
Measuring range (Urine)	11 - 333 (1+0) 110 - 3325 (1+9)	2.2 - 68 (1/1) 11 - 340 (1/5) 44 - 1360 (1/20) 220 - 6800 (1/100) 440 - 27200 (1/400)
Measuring range (CSF)	11 - 333 (1+0) 110 - 3325 (1+9)	2.2 - 68 (1/1) 11 - 340 (1/5) 44 - 1360 (1/20) 220 - 6800 (1/100) 440 - 27200 (1/400)
Measuring range (Serum)	2200 - 66500 (1+199)	350 - 5500 (1/20) 6900 - 110000 (1/100)

Differences		
Item	Test device	Predicate
Detection antibody	Sheep anti-human albumin	Rabbit anti-human albumin
Test method	Turbidimetry	Nephelometry
Open Vial Stability	3 months	4 weeks at 2-8°C
On-board stability	30 days	5 days at 8 hours/day for 5mL vials, 3 days at 8 hours/day for 2mL vials
Instrument	Binding Site Optilite	Siemens BNII

#### K. Standards and Guidance documents referenced:

CLSI EP17-A Protocols for Determination of Limits of Detection and Limits of Quantitation; Approved Guideline  
CLSI EP7-A2 Interference Testing in Clinical Chemistry, Approved Guideline - Second Edition  
CLSI EP6-A: Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach  
CLSI EP5-A2 Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline – Second Edition  
CLSI C28-A3: Defining, Establishing and Verifying Reference Intervals in the Clinical Laboratory

#### L. Test Principle:

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

#### M. Performance Characteristics (if/when applicable):

##### 1. Analytical performance:

##### a. *Precision/Reproducibility:*

The studies were based on CLSI EP5-A2, where 5 sample preparations for each matrix were tested in 2 runs per day (each of the 2 runs in duplicate) over 21 days using 3 analysers. Results met the Acceptance criteria for total precision (%CV<8.5%), within-run precision (%CV<5%), between-run precision (%CV<8.5%), between-day precision (%CV<8.5%) and between-instrument precision (%CV<10%). A summary of the results for each sample matrix is shown below; all results are in mg/L.

#### CSF Results:

Sample		1	2	3	4	5
N		84	84	84	84	84
Mean (mg/L)		145.5	281.5	439.9	593.1	975.2
Within Run	SD	0.98	3.55	3.72	5.81	13.81
	%CV	0.7	1.3	0.8	1.0	1.4
Between run	SD	1.44	2.19	6.85	7.08	25.08
	%CV	1.0	0.8	1.6	1.2	2.6
Between day	SD	8.59	14.79	14.18	19.13	74.82
	%CV	5.9	5.3	3.2	3.2	7.7
Between lot	SD	1.67	8.15	5.96	11.15	18.2
	%CV	1.15	2.89	1.36	1.88	1.87
Between instrument	SD	1.13	4.48	10.14	7.75	13.76
	%CV	0.77	1.59	2.3	1.3	1.41
Total	SD	8.77	15.37	16.18	21.21	80.11
	%CV	6.0	5.5	3.7	3.6	8.2

### Urine Results:

Sample		1	2	3	4	5
N		84	84	84	84	84
Mean (mg/L)		22.98	39.04	153.4	275.05	1490.18
Within Run	SD	0.15	0.22	1.54	2.12	13.33
	%CV	0.5	0.6	1.0	0.8	0.9
Between run	SD	0.57	0.68	1.29	3.7	22.3
	%CV	1.9	1.7	0.8	1.3	1.5
Between day	SD	0.67	1.04	2.5	7.78	29.35
	%CV	2.2	2.7	1.6	2.8	2.0
Between lot	SD	0.22	0.1	1.34	3.32	14.02
	%CV	0.97	0.26	0.87	1.21	0.94
Between instrument	SD	0.29	0.19	0.48	3.39	12.53
	%CV	1.24	0.5	0.31	1.23	0.84
Total	SD	0.89	1.26	3.21	8.87	39.2
	%CV	3.0	3.2	2.1	3.2	2.6

### Serum Results:

Sample		1*	2*	3	4	5
N		84	84	84	84	84
Mean (mg/L)		4012.8	14007.3	28501.1	36976.7	54447.2
Within Run	SD	73.33	179.16	340.92	478.12	866.65
	%CV	1.8	1.3	1.2	1.3	1.6
Between run	SD	96.21	289.26	261.4	314.41	843.34
	%CV	2.4	2.1	0.9	0.9	1.5
Between day	SD	132.07	526.46	713.95	791.26	1357.89
	%CV	3.3	3.8	2.5	2.1	2.5
Between lot	SD	.*	.*	281.8	235.27	324.17
	%CV	.*	.*	0.99	0.64	0.6
Between instrument	SD	102.12	526.57	152.98	195.66	767.86
	%CV	2.54	3.76	0.54	0.53	1.41
Total	SD	179.1	626.84	833.23	976.49	1818.29
	%CV	4.5	4.5	2.9	2.6	3.3

\* Samples 1 and 2 in the serum study used 4 instruments and one reagent lot. It is therefore not possible to calculate between-lot CV or SD.

#### *b. Linearity/assay reportable range:*

The studies followed CLSI EP6-A, whereby linearity was assessed across the curve width at the standard sample dilution (1+0 for CSF and urine and 1+199 for serum). The acceptance criteria were that the %CV for each sample should be  $\leq 8\%$  and the allowable nonlinearity was  $\pm 10\%$  or 10% of the medical decision point for each sample matrix.

A dilution series comprising a high pool and low pool for each sample matrix was tested in 3 replicates.

Weighted Linear Regression analysis was performed by plotting the % High Pool against the observed concentration, from which a weighted linear fit was generated for each point in the dilution series. This was then compared with the observed result and the difference calculated. Nonlinearity is less than 10% or 10% of the medical decision point in each sample matrix.



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

*i) Traceability:*

The calibration of the assay is traceable to ERM DA470k/IFCC.

*ii) Kit Stability:*

*Real-time stability* – Studies to establish shelf-life stability (from the date of manufacture when stored at recommended temperature 2-8°C) were performed on the 510(k)-cleared kit Human Albumin CSF Kit for use on SPAPLUS (K121045) demonstrating stability up to at least 18 months. This kit contains components manufactured using the same raw materials as the test device, with the exception of the high and low control materials, which are manufactured using a different buffer. Additional real time stability was therefore assessed using three manufacturing lots of control materials. Data supports an 18-month stability claim.

*Open-vial stability* - The Optilite Low Level Albumin Kit Reagent, Calibrator and Controls can be stored, opened at 2-8°C for up to 3 months.

*On-board stability* – The Optilite Low Level Albumin Kit Reagent can be stored on-board the Optilite Analyser for at least 30 days.

*d. Detection limit:*

The analytical sensitivity of both kits was determined in accordance with CLSI EP17-A. The Limit of Blank (LoB) was based on 60 determinations of a blank sample and was estimated as the 95% percentile of the distribution. The Limit of Detection (LoD) was calculated according to the equation  $LoB + 1.645 \times SDs$  where SDs, the standard deviation, was based on 12 determinations of 5 samples with analyte levels near the lower limit of the reportable range. Total error at LoQ was within the maximum allowable total error for each sample matrix.

**Urine and CSF:** The limit of quantitation (LoQ) for this assay is defined as the bottom of the measuring range, 11mg/L. The LoQ validation study was based on CLSI EP17-A *Protocols for Determination of Limits of Detection and Limits of Quantitation*.

**Serum:** The limit of quantitation (LoQ) for this assay is defined as the bottom of the measuring range, 2200mg/L. The LoQ validation study was based on CLSI EP17-A *Protocols for Determination of Limits of Detection and Limits of Quantitation*.

*e. Analytical specificity:*

Interferences were assessed according to CLSI EP7-A2 by testing samples for each sample matrix. Each sample was spiked with interfering substances and tested. For non-interference to be claimed, the mean results from the spiked samples must be within 10% of the mean of the control samples. The data demonstrated that the assay was not affected by the following substances at the concentrations given below.

**CSF results:**

Interferent	Rationale for inclusion	Concentration of interferent
Bilirubin	Endogenous substance.	200mg/L
Haemoglobin	Endogenous substance.	5g/L
Acetaminophen	Common OTC	1324µmol/L
Acetylsalicylic acid	Common OTC	3.63mmol/L

**Urine results:**

Interferent	Rationale for inclusion	Concentration of interferent
Ascorbic Acid	Common OTC	200mg/L
Haemoglobin	Endogenous substance.	250mg/L
Acetaminophen	Common OTC	1324µmol/L
Ibuprofen	Common OTC	2425µmol/L
Furosemide	Common drug used to treat oedema and hypertension	90µmol/L
Glybenclamide	Common drug used to treat Type 2 diabetes	3.89µmol/L
Trichloromethiazide	Common drug used to treat oedema and hypertension	50mg/mL
Metformin HCl	Common drug used to treat Type 2 diabetes	8mg/L
Enalapril Maleate	Commonly prescribed ACE inhibitor	496.7ng/mL
Losartan	Common drug used to treat hypertension	2932.08ng/mL
Simvastatin	Common drug used to treat hyperlipidaemia	12.9ng/mL
Acetone	Endogenous substance overproduced by diabetics	7000mg/L
Acetylsalicylic acid	Common OTC	1500mg/L
Calcium chloride	Food additive	780mg/L
Creatinine	Endogenous substance	6000mg/L
Glucose	Endogenous substance	30000mg/L
Magnesium chloride	Food additive	8000mg/L
Sodium citrate	Food additive	1000mg/L
Sodium oxalate	Associated with kidney stones	600mg/L
Urea	Endogenous substance	25g/L
Uric acid	Endogenous substance associated with diabetes	200mg/L
Urobilinogen	Endogenous substance	45mg/L

Metronidazole is known to interfere at a concentration of 375mg/L.

**Serum results:**

Interferent	Rationale for inclusion	Concentration of interferent
Bilirubin	Endogenous substance.	200mg/L
Haemoglobin	Endogenous substance.	5g/L
Acetaminophen	Common OTC	1324µmol/L
Acetylsalicylic acid	Common OTC	3.63mmol/L
Intralipid	Endogenous substance.	2000mg/dL
Triglycerides	Endogenous substance.	1000mg/dL

*f. Assay cut-off:*

Not determined

*g. Antigen Excess Effects:*

Antigen excess was evaluated with serum samples of up to 67384mg/L run at the 1+0 (neat) sample dilution. This is approximately 200 times the top of the calibration curve. Antigen excess was correctly detected and flagged by the analyser in all cases.

2. Comparison studies:

*a. Method comparison with predicate device:*

Samples were tested in singlicate.

Sample Matrix	Number of samples	Within reference interval	Outside reference interval
CSF	166	110	56
Urine	191	109	82
Serum	142	84	58

Analyte	Passing Bablok Regression Equation	Slope (95% CI)	Intercept (95% CI)	r value (from linear regression)
CSF	1.00x + 11.76	0.97 to 1.03	6.16 to 16.83	0.988
Urine	1.06x - 0.44	1.04 to 1.07	-1.28 to 0.31	0.994
Serum	1.01x + 932.82	0.97 to 1.05	-391.08 to 2304.62	0.996

*b. Matrix comparison:*

None

3. Clinical studies:

*a. Clinical Sensitivity:*

None determined

*b. Clinical specificity:*

None determined

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

Not applicable

4. Clinical cut-off:

These are based on the limits of the reference range for each sample matrix, as follows:

Urine: <30mg/L

CSF: <350mg/L.

Serum: 35000 - 52000mg/L

5. Expected values/Reference range:

The urine and serum reference ranges were transferred from the predicate devices and were verified by testing 50 adult donor samples for each matrix. The reference range for albumin in CSF is taken from literature in common with the predicate device.

Urine: <30mg/L

CSF: <350mg/L.

Serum: 35000 - 52000mg/L

**N. Proposed Labelling:**

The labelling 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.