October 12, 2018

The Binding Site Group Ltd
Andrea Thomas, Regulatory Affairs Manager
8 Calthorpe Road
Edgbaston
Birmingham
B15 1QT
UK

Re: K180099
Trade/Device Name: Optilite High Sensitivity C-Reactive Protein Kit
Regulation Number: 21 CFR 866.5270
Regulation Name: C-reactive protein immunological test system
Regulatory Class: Class II
Product Code: DCN
Dated: August 29, 2018
Received: September 4, 2018

Dear Andrea Thomas:

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. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database located at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm identifies combination product submissions. 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 Part 801 and Part 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803) for devices or postmarketing safety reporting (21 CFR 4, Subpart B) for combination products (see https://www.fda.gov/CombinationProducts/GuidanceRegulatoryInformation/ucm597488.htm); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

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 comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/) and CDRH Learn (http://www.fda.gov/Training/CDRHLearn). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (http://www.fda.gov/DICE) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Kellie B. Kelm -S

for Courtney H. Lias, Ph.D.
Director
Division of Chemistry and Toxicology Devices
Office of In Vitro Diagnostics
and Radiological Health
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: 06/30/2020
See PRA Statement below.

510(k) Number *(if known)*
K180099

Device Name
Optilite High Sensitivity C-Reactive Protein Kit

Indications for Use *(Describe)*
The Optilite High Sensitivity C-Reactive Protein Kit is intended for the quantitative in vitro measurement of C-Reactive Protein in serum using the Binding Site Optilite analyser for evaluation of conditions thought to be associated with inflammation, in otherwise healthy individuals. 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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Optilite High Sensitivity C-Reactive Protein Kit
510(k) Summary

Date prepared: 11th October 2018

A. 510(k) Number:

K180099

B. Purpose for Submission:

New device

C. Measurand:

C-Reactive Protein

D. Type of Test:

Quantitative immunoturbidimetry

E. Applicant:

The Binding Site Group, Ltd.
Contact person: Andrea Thomas
Address: 8 Calthorpe Road, Birmingham, B15 1QT, United Kingdom
Contact number: +44(0)121 456 9500

F. Proprietary and Established Names:

Optilite® High Sensitivity C-Reactive Protein Kit

G. Regulatory Information:

1. Regulation section:

   21 CFR 866.5270, C-reactive protein immunological test system.

2. Classification:

   Class II

3. Product code:

   DCN, System, Test, C-Reactive Protein

4. Panel:

   Immunology (82)

H. Intended use:

1. Intended use(s):

The Optilite High Sensitivity C-Reactive Protein Kit is intended for the quantitative in vitro measurement of C-Reactive Protein in serum using the Binding Site Optilite analyser for evaluation of conditions thought to be associated with inflammation, in otherwise healthy individuals. This test should be used in conjunction with other laboratory and clinical findings.

2. Indication(s) for use:

Same as Intended use(s).

3. Special conditions for use statement(s):

Prescription use only

4. Special instrument requirements:

The Binding Site Optilite analyser

I. Device Description:

The Optilite High Sensitivity C-Reactive Protein Kit is comprised of latex reagent, single calibrator, controls (high and low) and reaction buffer in liquid form. The reagents contain 0.099% sodium azide as preservative.

J. Substantial equivalence information:

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

C-Reactive Protein High Sensitive Test System for Cobas Integra Instruments (K053603)

2. Comparison with predicate:

Similarities

Item	Device	Predicate
Intended use	Quantitative in vitro measurement of C-reactive protein (CRP)	Same
Reference Interval	<3mg/L	<5mg/L
Sample type	Serum	Serum (also Li-heparin and EDTA plasma)
Reagent type	Latex enhanced	Same
Open vial stability	Three months at 2 to 8°C	12 weeks (on-board)
Method	Turbidimetry	Same

Differences

Item	Device	Predicate
Measuring Range	0.5-10mg/L (neat)	0.1-20.0mg/L 1.5-300mg/L (1/15 dilution)
Analyser	Optilite	Integra
Antibody	anti- human CRP (sheep)	anti-human CRP (mouse)
On board stability	30 days (refrigerated on analyser)	12 weeks
Calibration	6 point, single calibrator diluted on analyser	5 point, calibrator set
Traceability	DA474	ERM-DA470 (CRM470)

K. Standards and Guidance documents referenced:

Guidance for Industry - Review Criteria for Assessment of C - Reactive Protein (CRP), High Sensitivity C-Reactive Protein (hsCRP) and Cardiac C-Reactive Protein (cCRP) Assays Guidance for Industry and FDA Staff

CLSI EP17-A2 Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline – Second Edition

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-A3 Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline – Third Edition

L. Test Principle:

The determination of soluble antigen (CRP) concentration by turbidimetric methods involves the reaction with specific antiserum (anti-CRP) 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-A3, where 5 sera samples (targeted at 1mg/L, 1-3mg/L, 3mg/L, 5mg/L, and 9mg/L) were tested in 2 runs per day (each of the 2 runs in duplicate) over 21 days using 3 reagent lots on 3 analysers. Results met the acceptance criteria for total precision (%CV<10%), within-run precision (%CV<5%), between-run precision (%CV<8%), and between-day precision (%CV<8%).

Sample		1	2	3	4	5
Mean concentration (mg/L)		0.98	1.55	2.99	5.41	8.50
Total precision	SD	0.055	0.077	0.134	0.237	0.260
	%CV	5.6	5.0	4.5	4.4	3.1
Within-run precision	SD	0.029	0.024	0.047	0.115	0.168
	%CV	2.9	1.5	1.6	2.1	2.0
Between-run precision	SD	0.000	0.021	0.069	0.081	0.000
	%CV	0.0	1.4	2.3	1.5	0.0
Between-day precision	SD	0.047	0.070	0.104	0.191	0.199
	%CV	4.8	4.5	3.5	3.5	2.3
Between-batch precision	SD	0.011	0.022	0.057	0.131	0.137
	%CV	1.1	1.4	1.9	2.4	1.6
Between-instrument precision	SD	0.047	0.054	0.068	0.113	0.100
	%CV	4.7	3.5	2.3	2.1	1.2

b. Linearity/assay reportable range:

A linearity study was performed following CLSI EP6-A. The linearity of the high sensitivity CRP assay has been confirmed using serially diluted serum samples to cover the standard measuring range of 0.5 – 10.0 mg/L. The results demonstrated that the high sensitivity CRP assay is linear over the ranges of 0.44 – 12.16 mg/L at 1+0 dilution with deviation from linearity ≤ 10%.

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

i) *Traceability*:

The calibration of the assay is traceable to the international reference standard ERM- DA474.

ii) Kit Stability:

Real-time stability – A study to establish shelf-life stability (from the date of manufacture when stored at recommended temperature 2-8°C) of the Optilite High Sensitivity CRP Kit is on-going. Currently available data supports a 13 month stability claim.

Open-vial stability - The Optilite High Sensitivity CRP Kit can be stored, opened at 2 – 8°C for up to 3 months.

On-board stability – The Optilite High Sensitivity CRP Kit can be stored on-board the Optilite Analyser for at least 30 days.

d. Detection limit:

The analytical sensitivity was determined in accordance with CLSI EP17-A2. The Limit of Blank (LoB) was based on 4 serum samples run 5 times per day, over 3 days, on 3 reagent lots to give a total of 60 results per lot. The LoB was estimated for each lot as the 95th percentile of the distribution.

The Limit of Detection (LoD) was based on 4 serum samples run 5 times per day, over 3 days, on 3 reagent lots to give a total of 60 results per lot. The LoD calculation followed parametric analysis.

The LoQ was determined from 4 serum samples targeted to be close to the bottom of the measuring range, tested 5 times per day over 3 days on 2 reagent lots.

For LoB and LoD, the highest result obtained from the two lots tested was taken as the final result (see below):

LoB	LoD	LoQ
0.15mg/L	0.17mg/L	0.5mg/L

e. Analytical specificity:

Interferences were assessed according to CLSI EP7-A2 by testing serum samples with CRP concentrations targeted at <1mg/L, 1-3mg/L, 3mg/L and >3mg/L. 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.

Haemoglobin and Bilirubin results: The data demonstrated that the assay was not affected by high levels of the following substances: haemoglobin (5g/L), conjugated bilirubin (200mg/L) unconjugated bilirubin (200mg/L) and rheumatoid factor (25IU/mL).

Intralipid and Triglyceride results: The data demonstrated that the assay was not affected by triglyceride (1000mg/dL), and intralipid (2000mg/dL).

Drug Interference results: The data demonstrated that the assay was not affected by the 6 therapeutic drugs tested at the concentrations given below.

Drug	Concentration tested
Acetaminophen	1324µmol/L
Acetylsalicylic Acid	3.62mmol/L
Caffeine	308µmol/L
Enalapril Maleate	0.86µmol/L
Ibuprofen	2425µmol/L
Warfarin	32.5µmol/L

f. Assay cut-off:

Refer to Expected Values.

2. Comparison studies:

a. Method comparison with predicate device:

A total of 391 serum samples, 302 of which reported results within the measuring range, were assayed in singlicate by both the Optilite High Sensitivity C-Reactive Protein Kit and the C-Reactive Protein High Sensitive Test System for Cobas Integra. The samples included 87 normal donors and 304 clinical samples.

Regression statistics are based on the balance of the paired results.

Results (n = 302)				
Analysis	**Result**	**95% CI Slope**	**95% CI Intercept**	**Pass/Fail**
Passing & Bablok	y = 0.99x + 0.09	0.97 to 1.01	0.05 to 0.11	PASS
Weighted Deming	y = 0.97x + 0.10	0.94 to 0.99	0.07 to 0.13	
Weighted Linear	y = 0.95x + 0.12	0.93 to 0.98	0.10 to 0.15	

b. Matrix comparison:

None

3. Clinical studies:

a. Clinical Sensitivity:

Not applicable

b. Clinical specificity:

Not applicable

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

Not applicable

4. Clinical cut-off**:**

Not applicable

5. Expected values/Reference range:

The reference interval was verified by testing 50 adult donor samples.

Consensus reference interval for adults: <3 mg/L
Reference: Macy EM, Hayes TE, Tracy RP. Variability in the measurement of C-Reactive protein in healthy subjects; implications for reference intervals and epidemiological applications. Clin Chem 1997; 43: 52-8.

N. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

O. Conclusion:

The summary includes the conclusions drawn from the nonclinical and clinical tests (discussed above) that demonstrate that the device is as safe, as effective, and performs as well as or better than the predicate device