DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
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April 5, 2017

The Binding Site Group Ltd
Ms. Kirsty Samuels
Regulatory Affairs Officer
8 Calthorpe Road, Edgbaston
Birmingham, West Midlands, B15 1QT
UK

Re: K161982
Trade/Device Name: C-Reactive Protein Kit for Use on SPAPlus
Regulation Number: 21 CFR 866.5270
Regulation Name: C-Reactive Protein Immunological Test System
Regulatory Class: II
Product Code: DCN
Dated: March 9, 2017
Received: March 10, 2017

Dear Ms. Samuels:

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 regulations (21 CFR Parts 801 and 809), 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 yours,

Kelly Oliner -S

FOR
Leonthena R. Carrington, MS, MBA, MT(ASCP)
Director
Division of Immunology and Hematology 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: January 31, 2017
See PRA Statement below.

510(k) Number *(if known)*
K161982

Device Name
C-Reactive Protein Kit for use on SPAPLUS

Indications for Use *(Describe)*
The C-Reactive Protein Kit for use on SPAPLUS is intended for the quantitative in vitro determination of C-reactive protein (CRP) concentration in serum. Measurement of C-reactive protein aids in evaluation of the amount of injury to body tissues and for evaluation of infection, tissue injury, and inflammatory disorders. This product is suitable for use on the SPAPLUS analyser.

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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C-Reactive Protein kit for use on SPAPLUS
510(k) Summary

A. 510(k) Number:

K161982

B. Purpose for Submission:

New device

C. Measurand:

C-Reactive Protein

D. Type of Test:

Quantitative immunoturbidimetry

E. Applicant:

The Binding Site

F. Proprietary and Established Names:

C-Reactive Protein Kit for use on SPAPLUS®

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 C-Reactive Protein Kit for use on SPAPLUS is intended for the quantitative in vitro determination of C-reactive protein (CRP) concentration in serum.

2. Indication(s) for use:

Measurement of C-reactive protein aids in evaluation of the amount of injury to body tissues and for evaluation of infection, tissue injury, and inflammatory disorders. This product is suitable for use on the SPAPLUS analyser.

3. Special conditions for use statement(s):

Prescription use only

4. Special instrument requirements:

The Binding Site SPAPLUS analyser

I. Device Description:

The C-Reactive Protein Kit for use on SPAPLUS is comprised of the following reagents:

Antiserum: Supplied in stabilised liquid form. Preservatives: 0.099% sodium azide, TRIS pH 8.0.

Calibrator and Controls: Pooled human serum, supplied in stabilised liquid form. Containing 0.099% sodium azide, as preservative. The concentration given on the quality control certificate has been obtained by comparison with the international reference standard ERM-DA474.

Reaction Buffer: Containing 0.099% sodium azide, TRIS pH 7.5 as preservatives.

J. Substantial equivalence information:

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

Roche Diagnostics Tina-Quant C-Reactive Protein Gen. 3 (K083444)

2. Comparison with predicate:

Similarities

Item	Device	Predicate
Intended use	Quantitative in vitro determination of C-reactive protein (CRP).	Same.
Method	Turbidimetry	Same.
Reference Interval	<5mg/L	Same.
Sample type	Serum	Serum (also Li-heparin and EDTA plasma)

Differences

Item	Device	Predicate
Measuring Range	5-250mg/L (neat) 50-2500mg/L (1/10 dilution)	0.3-350mg/L (neat) 0.6-700mg/L (1/2 dilution)
Analyser	SPAPLUS	Hitachi 912, 917, Modular P
Antibody	anti- human CRP (goat)	anti-human CRP (mouse)
Open vial stability	Three months at 2 to 8°C	Not stated.
On board stability	30 days.	84 days opened and refrigerated on the analyser.
Reagent	Antiserum	Latex particles coated with anti-CRP (mouse)
Calibration	5 point, calibrator set	5 point, single calibrator diluted on analyser
Wavelength	340nm	570nm/800nm
Traceability	ERM-DA474	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-A2 Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline – Second 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-A2, where 4 sera samples (targeted to 6.025mg/L, 8.643mg/L, 21.342mg/L and 65.165mg/L) were tested in 2 runs per day (each of the 2 runs in duplicate) over 21 days using 1 reagent lot 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
Mean concentration (mg/L)		6.025	8.643	21.342	65.165
Total precision	SD %CV	0.5086 8.4	0.6111 7.1	0.5320 2.5	1.2034 1.8
Within-run precision	SD %CV	0.1129 1.9	0.1102 1.3	0.1314 0.6	0.3034 0.5
Between-run precision	SD %CV	0.2723 4.5	0.3262 3.8	0.4082 1.9	1.1645 1.8
Between-day precision	SD %CV	0.4144 6.9	0.5049 5.8	0..3147 1.5	0.0000 0.0
Between-instrument precision	SD %CV	0.335 5.6	0.529 6.0	0.037 0.2	0.434 0.7

b. Linearity/assay reportable range:

The studies followed CLSI EP6-A, whereby linearity was assessed across the curve width at the standard sample dilution (1/1).

The acceptance criteria were that the %CV for each sample should be ≤8% and the allowable nonlinearity was ± 10%.

A series of 13 samples was tested in 3 replicates. Results met the Acceptance criteria for CV<8%.

% High pool	Mean Result	SD	%CV
100.0%	315.333	2.574	0.8
90.0%	288.100	5.110	1.8
80.0%	258.867	3.313	1.3
70.0%	224.033	1.457	0.7
60.0%	198.900	3.175	1.6
50.0%	176.533	0.902	0.5
40.0%	144.433	1.250	0.9
30.0%	108.233	1.079	1.0
20.0%	71.400	0.265	0.4
10.0%	35.167	0.681	1.9
1.5%	5.700	0.100	1.8
1.0%	4.133	0.058	1.4
0.5%	2.800	0.000	0.0

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 SPAPLUS CRP Kit is on-going. Currently available data supports a 5-month stability claim.

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

On-board stability – The SPAPLUS CRP Kit reagents 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 60 determinations of a blank sample and was estimated as the 95% percentile of the distribution. The LoQ study was carried out on two reagent lots. The highest LoQ from the results of the two reagent lots was used as the overall LoQ result. The highest LoD calculated from the two LoQ studies was used as the overall LoD.

The Limit of Detection (LoD) was calculated for both reagent lots according to the equation: the LoB + 1.645 x SD where SD was based on the standard deviation of the sample used for the LoQ claim.

The LoQ was calculated and the total error % (12%) was within the maximum allowable total error.

LoB	LoD	LoQ
0.5mg/L	0.7529mg/	5.0mg/L

e. Analytical specificity:

Interferences were assessed according to CLSI EP7-A2 by testing serum samples with CRP concentrations falling above (elevated) (target 60mg/L and 150mg/L) or close to the limits of the reference interval (target 5mg/L). Each sample was spiked with interfering substances and tested in replicates of 3. 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, Bilirubin and RF results: The data demonstrated that the assay was not affected by high levels of the following substances: haemoglobin (5g/L), bilirubin (200mg/L) and Rheumatoid Factor (RF) (2417IU/mL).

Intralipid results: The data demonstrated that the assay was not affected by intralipid at the level of 250mg/dL.

Drug Interference results: The data demonstrated that the assay was not affected by the 14 therapeutic drugs tested at the concentrations given below.

Drug	Concentration tested
Acetaminophen	1324µmol/L
Acetylsalicylic Acid	1.95mmol/L
Amoxicillin	206µmol/L
Ascorbic Acid	342µmol/L
Caffeine	308µmol/L
Cefotaxime	673µmol/L
Theophylline	222µmol/L
Chloramphenicol	155µmol/L
Cimetidine	79.2µmol/L
Digoxin	7.8nmol/L
Fluconazole	245µmol/L
Ibuprofen	606.25µmol/L
Penicillin	75mg/L
Phenytoin	198µmol/L

f. Assay cut-off:

Not applicable

2. Comparison studies:

a. Method comparison with predicate device:

A total of 225 serum samples spanning the dynamic range were assayed in singlicate by both the CRP Kit on the SPAPLUS Analyser and the Tina-Quant C-Reactive Protein Gen. 3 assay for use on the Modular P analyser. The samples included 82 normal donors and 143 clinical samples.

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

Regression fit	**Regression Equation**	**Slope (95% CI)**	**Intercept (95% CI)**
Weighted Linear	Y = 1.064x + 1.14	1.05 to 1.08	0.89 to 1.40
Passing-Bablok	Y = 1.021x + 3.22	1.01 to 1.04	2.32 to 4.27
Weighted Deming	Y = 1.062x + 1.13	1.05 to 1.08	0.74 to 1.52

99.6% of samples tested gave clinically concordant results on both analysers.

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:

Consensus reference interval for adults: <5 mg/L

Reference: Dati F, Schumann G, Thomas L et al. Consensus of a group of professional societies and diagnostic companies on guidelines for interim reference ranges for 14 proteins in serum based on the standardization against the IFCC/BCR/CAP reference material (CRM 470). Eur J. Clin Chem Clin Biochem 1996;34:517-520.

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.