September 4, 2019

The Binding Site Group Ltd
Natasha Verhaak
Regulatory Affairs Officer
8 Calthorpe Road Edgbaston
Birmingham, B15 1QT Gb

Re: K192116
Trade/Device Name: Human IgA liquid reagent kit for use on SPAPLUS
Regulation Number: 21 CFR 866.5510
Regulation Name: Immunoglobulins A, G, M, D, And E Immunological Test System
Regulatory Class: Class II
Product Code: CFN
Dated: June 30, 2019
Received: August 6, 2019

Dear Natasha Verhaak:

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/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products); 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 https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance) and CDRH Learn (https://www.fda.gov/training-and-continuing-education/cdrh-learn). 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 (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/contact-us-division-industry-and-consumer-education-dice) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Douglas Jeffery, Ph.D.
Chief
Division of Immunology
and Hematology Devices
OHT7: Office of In Vitro Diagnostics
and Radiological Health
Office of Product Evaluation and Quality
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)*
K192116

Device Name
Human IgA liquid reagent kit for use on SPAPLUS

Indications for Use *(Describe)*

This kit is intended for the quantitative in vitro determination of human IgA in serum, lithium heparin or EDTA plasma, using the Binding Site SPAPLUS turbidimetric analyser. Measurement of IgA aids 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.

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.

This section applies only to requirements of the Paperwork Reduction Act of 1995.

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Human IgA Kit for Use on SPAPlus
Special 510(k) Submission Summary

Submitter Details
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Date Prepared: *28th August 2019*

A. 510(k) Number:
K192116

B. Purpose for Submission:
Modification to an existing device

C. Measurand:
IgA

D. Type of Test:
Quantitative immunoturbidimetry

E. Applicant:
The Binding Site

F. Proprietary and Established Names:
Human IgA liquid reagent kit for use on 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:
   CFN – method, nephelometric, immunoglobulins (G, A, M)

4. Panel:
   Immunology (82)

H. Intended use:

1. Intended use(s):

This kit is intended for the quantitative in vitro determination of human IgA in serum, lithium heparin or EDTA plasma, using the Binding Site SPAPLUS turbidimetric analyser. Measurement of IgA aids 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.

The intended use is the same as the cleared kit and has not been changed.

3. Indication(s) for use:

Same as Intended use.

3. Special conditions for use statement(s):

Prescription use only

3. Special instrument requirements:

The Binding Site SPAPlus analyser

I. Device Description:

Human IgA liquid reagent kit for use on SPAPLUS® comprises the following reagents:

Antiserum: Monospecific goat anti IgA supplied in stabilised liquid form.
It contains 0.099% sodium azide, 0.1% E-amino-n-caproic acid (EACA), 0.5% BSA and 0.01% benzamidine as preservatives.

Calibrator and Controls: These consist of pooled human serum and are supplied in stabilised liquid form. The concentration of IgA given on the quality control certificate has been obtained by comparison with European Reference Material ERM-DA470k. They contain 0.099% sodium azide, 0.1% EACA and 0.01% benzamidine as preservatives.

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

J. Substantial equivalence information:

1. Predicate device name(s) and 510(k) number(s):
Human IgA liquid reagent kit for use on SPAPLUS® (K103824)

2. Comparison with predicate:

Similarities		
Item	**Modified device**	**Registered device**
Intended Use	Quantitative in vitro measurement of IgA	Same
Test Method	Turbidimetric	Same
Specimen Type	Serum, lithium heparin, EDTA plasma	Same
Assay type	Quantitative	Same
On-board Stability	30 days	Same
Calibration traceability	DA470k	Same
Measuring Range	1/1 0.02 – 0.70 g/L **1/10 0.20 - 7.00 g/L** 1/40 0.80 – 28.00 g/L Where results are greater than the measuring range samples should be rerun at 1/10 with a manual offline dilution of 1/10 to give an overall dilution of 1/100.	Same
Adult Reference Interval	0.845 – 4.990 g/L	Same
Instrument	SPAPlus	Same
Antigen excess capacity	40 g/L	Same
Calibration method	Calibrator set consisting of pooled human sera	Same
Controls	low and high, consisting of pooled human sera	Same
Open vial stability	3 months	Same
Antibody processing	Affinity purification, specificity confirmed by IEP	Same
Antibody resting buffer	GBS	Same

Differences		
Item	**Modified device**	**Registered device**
Source of detection antibody	Goat antibody	Sheep antibody

K. Standards and Guidance documents referenced:

CLSI EP17-A2 Protocols for Determination of Limits of Detection and Limits of Quantitation; Approved Guideline
CLSI EP5-A3 Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline – Second Edition
CLSI EP25-A Evaluation of Stability of In Vitro Diagnostic Reagents- 1st Edition
CLSI EP6-A Evaluation of the Linearity of Quantitative Measurement Procedures
EP28- A3c Defining, Establishing, and Verifying Reference Intervals in the Clinical Laboratory, 3rd Edition

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 precision studies were based on CLSI EP5-A3 *Evaluation of Precision Performance of Clinical Quantitative Measurement Methods* as was agreed in pre-submission meeting Q171503.

The repeatability and within laboratory study was performed over 20 working days, with 2 runs per day and 2 replicates per run. 4 different samples were assessed using 1 reagent lot on 1 analyser.

Repeatability and Within Laboratory Results:

Repeatability and Within Laboratory Summary										
	N	Mean (g/L)	Within run		Between run		Between day		Total	
			SD	CV %	SD	CV %	SD	CV %	SD	CV %
Level 1	80	5.750	0.109	1.9	0.120	2.1	0.111	1.9	0.196	3.4
Level 2	80	3.495	0.059	1.7	0.095	2.7	0.032	0.9	0.117	3.3
Level 3	80	0.346	0.012	3.4	0.017	4.9	0.013	3.7	0.024	7.1
Level 4	80	0.095	0.003	3.0	0.000	0.0	0.003	2.8	0.004	4.1

The between instrument precision study was performed over 6 working days. 2 instruments were tested each day with 2 replicates per instrument. 4 different samples were assessed using 1 reagent lot on 3 different analysers.

Between Instrument Results:

	N	Mean (mg/L)	Between Instrument	
			SD	CV %
Level 1	24	5.716	0.031	0.5
Level 2	24	3.546	0.050	1.4
Level 3	24	0.356	0.000	0.0
Level 4	24	0.096	0.002	1.8

The between lot precision study was performed over 6 working days. 2 lots were tested each day with 2 replicates per lot. 4 different samples were assessed using 3 reagent lots on 1 analyser.

Between Lot Results:

	N	Mean (mg/L)	Between Lot	
			SD	CV %
Level 1	24	5.746	0.000	0.0
Level 2	24	3.550	0.000	0.0
Level 3	24	0.360	0.012	3.2
Level 4	24	0.098	0.003	2.7

The above results do not indicate any change in performance compared to the device cleared in K103824. The precision claims in the product insert therefore still accurately represent the performance of the modified kit and do not need to be amended.

b. Linearity/assay reportable range:

A linearity study was carried out as per the original submission (K103824). A dilution series was produced from a high pool with a known concentration of 8.19g/L and a low pool concentration of 0.12 g/L. Each diluted sample was tested in 3 replicates and a linear regression analysis was carried out. The linear regression equation was shown to be y=0.993x - 0.230 g/L with an R value of 0.996.

These results are comparable to those currently presented in the product insert and therefore do not indicate any change in performance compared to the device cleared in K103824. The linearity claims in the product insert therefore still accurately represent the performance of the modified kit and do not need to be amended.

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:

Accelerated Stability

Accelerated stability studies were carried out to verify that the stability of the kit is unchanged in accordance with ISO 23640:2015. 6 replicates of controls, internal reference and samples were tested over a period equivalent to 19 months and analysed in line with EP25-A with a maximum allowable difference of ±15% in order to verify the stability claim of 18 months. Reagents were stored at 37^0C to accelerate the study by a factor of 10.

Accelerated Stability Results

Batch 455406

Parameter	IR	Control		Sample		
		Low	High	1	2	3
Accelerated stability achieved (days)	57	57	57	57	57	57
Equivalent at 4^0C (days)	561	561	561	561	561	561
Stability required at 4^0C (days)	395	395	395	395	395	395
Decision	Pass	Pass	Pass	Pass	Pass	Pass

Batch 455407

Parameter	IR	Control		Sample		
		Low	High	1	2	3
Accelerated stability achieved (days)	57	57	57	57	57	57
Equivalent at 4^0C (days)	561	561	561	561	561	561
Stability required at 4^0C (days)	395	395	395	395	395	395
Decision	Pass	Pass	Pass	Pass	Pass	Pass

Real Time Stability

To further support the results of the accelerated stability testing, a real time stability study is currently being carried out in accordance with EP25-A and as was agreed in pre-submission meeting Q171503.

On Board Stability

On-board stability studies were carried out as per the original submission and showed no difference in the cleared on-board stability claim

d. Detection limit:

The limit of quantitation (LoQ) for this assay is defined as the bottom of the measuring range, 0.02 g/L. The LoQ validation study was based on CLSI EP17-A2 Evaluation of the Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline – 2nd Edition in accordance with pre-submission meeting Q171503. Four samples were tested using two reagent lots. The LoQ claim was validated by all the samples reporting within the acceptance criteria of an allowable CV of 8%.
The limit of detection (LoD) represents the lowest measurable analyte level that can be distinguished from zero, this was estimated as 0.003 g/L in the original submission and the limit of blank (LoB) was estimated to be 0.001 g/L. Additional testing was carried out following the antisera change and no change in performance was observed.

The results generated do not indicate any change in performance compared to the device cleared in K103824. The LoB, LoD and LoQ claims in the product insert therefore still accurately represent the performance of the modified kit and do not need to be amended.

e. Analytical specificity:

As per original submission (K103824)

f. Assay cut-off:

Not determined

3. Comparison studies:

a. Method comparison with predicate device:

A comparison study was performed by analysing 102 serum samples, 42 plasma samples using the modified SPAPlus IgA Kit and the cleared SPAPlus kit which is already commercially available. The study was carried out in accordance with pre-submission meeting Q171503. Bland Altman and Passing Bablok regression analysis generated the following results:

Bland Altman Mean Bias	95% Limits of Agreement
-2.18%	0.55% to 3.17%

Passing Bablok	Slope 95% CI	Intercept 95% CI
y= 1.017x + 0.002	1.004 to 1.029	-0.029 to 0.026

Correlation coefficient
0.998

Predicate Sample Range (g/L)	Test Samples Range (g/L)
0.038 – 18.26	0.050 – 18.57

The above results do not indicate any change in performance compared to the device cleared in K103824. The comparison claims in the product insert therefore still accurately represent the performance of the modified kit and do not need to be amended.

b. Matrix comparison:

Serum and plasma matrices were included in the above method comparison study. As per the original submission (K103824), no difference between matrices were observed.

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**:**

None determined

5. Expected values/Reference range:

Following the protocol agreed in Q171503, 20 samples from apparently healthy US donors were tested using the modified assay. The acceptance criteria for the transfer is ≤2 samples falling outside of the limits of the reference interval to be transferred.

Of the 20 samples tested, all 20 gave results within the reference interval, ranging from 1.553 to 4.840 g/L. The results of this study therefore meet the acceptance criteria and indicate that the reference interval can be transferred from the originally cleared device.

N. Proposed Labelling:

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

The labelling is the same as the cleared kit and has not been changed.

O. Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.