DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
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January 7, 2015

QUALIGEN, INC.
MICHAEL POIRIER
SENIOR VICE PRESIDENT, CSO/CTO
2042 CORTE DEL NOGAL
CARLSBAD CA 92011

Re: K141689
Trade/Device Name: Fastpack High Sensitivity C-reactive Protein Immunoassay
Fastpack High Sensitivity C-reactive Protein Calibrator Kit
Fastpack High Sensitivity C-reactive Protein Controls,
Fastpack High Sensitivity C-reactive Protein Method Verification Kit
Regulation Number: 21 CFR 866.5270
Regulation Name: C-reactive protein immunological test system
Regulatory Class: II
Product Code: DCK, JIT, JJX
Dated: December 15, 2014
Received: December 18, 2014

Dear Mr. Poirier:

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,

Katherine Serrano -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: January 31, 2017
See PRA Statement below.

510(k) Number *(if known)*
K141689

Device Name
FastPack® High Sensitivity C-Reactive Protein Immunoassay, FastPack® High Sensitivity C-Reactive Protein Calibrator Kit, FastPack® High Sensitivity C-Reactive Protein Controls, FastPack® High Sensitivity C-Reactive Protein Method Verification Kit

Indications for Use *(Describe)*

FastPack® High Sensitivity C-Reactive Protein Immunoassay is to be used for evaluation of conditions thought to be associated with inflammation, in otherwise healthy individuals. The FastPack® High Sensitivity C-Reactive Protein Immunoassay is intended for use with the FastPack® Analyzer. Not intended for Point-of-Care use.

FastPack® High Sensitivity C-Reactive Protein Calibrators are used for calibrating the quantitative FastPack® High Sensitivity C-Reactive Protein Immunoassay on the FastPack® Analyzer.

FastPack® High Sensitivity C-Reactive Protein Controls are used for quality control of the FastPack® High Sensitivity C-Reactive Protein Immunoassay on the FastPack® Analyzer.

FastPack® High Sensitivity C-Reactive Protein Verifiers are used in the quantitative verification of calibration and assay range of the quantitative FastPack® High Sensitivity C-Reactive Protein Immunoassay on the FastPack® Analyzer.

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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510(k) SUMMARY

REVISED
510(k) SUMMARY

This 510(k) Summary information is submitted in accordance with the requirements of 21 CFR § 807.92.

510(k) Number: K141689

Submitter:

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Device Identification

Trade Names: FastPack® High Sensitivity C-Reactive Protein Immunoassay
FastPack® High Sensitivity C-Reactive Protein Calibrator Kit
FastPack® High Sensitivity C-Reactive Protein Controls
FastPack® High Sensitivity C-Reactive Protein Method Verification Kit

Common Names: C-reactive protein Assay
C-reactive protein Calibrator
C-reactive protein Controls
C-reactive protein Verifiers

Classification names: Immunological Test Systems
Calibrator
Quality control material (assayed and unassayed)

Classifications: Class II (assay)

Class II (calibrators)
Class I, reserved (controls)
Class I, reserved (verifiers)

Panel: Chemistry (75)

Product Codes: DCK - C-Reactive Protein, Antigen, Antiserum
JIT - Calibrator, Secondary
JJX - Quality control material (Assayed and Unassayed)

Regulation Numbers: 21 CFR § 866.5270 - C-reactive protein immunological test system
21 CFR § 862.1150 - Calibrator
21 CFR § 862.1660 - Quality control material (Assayed and Unassayed)

Devices to Which Substantial Equivalence is Claimed

Olympus CRP Latex reagent
Olympus America, Inc.
3500 Corporate Parkway
PO Box 610
Center Valley, PA
K051564

Liquichek™ Cardiac Markers Plus Control
Bio-Rad Laboratories
4000 Alfred Nobel Drive
Hercules, CA 94547
K050537

VITROS Chemistry Products hsCRP Performance Verifier I, II, and III
Ortho-Clinical Diagnostics, Inc.
100 Indigo Creek Drive
Rochester, NY 14626-5101
K041799

Device Description

The FastPack® High Sensitivity C-Reactive Protein Immunoassay employs a Sandwich immunoassay principle. Endogenous CRP in a patient sample, calibrator, control, or verifier is dispensed into a FastPack® reagent pack. In the reagent pack, the sample binds with a monoclonal anti-CRP antibody covalently linked to alkaline

phosphatase (ALP) and a different monoclonal anti-CRP antibody linked to biotin. After incubation, immunoreacted complex (Monoclonal anti-CRP antibody-ALP conjugate and anti-CRP antibody linked to biotin reacted with CRP in the sample) is mixed with streptavidin coated paramagnetic particles. After washing steps (using a Tris buffer containing detergents) to separate bound from unbound anti-CRP monoclonal antibody-ALP, a chemiluminogenic substrate mixture is added to the system. This mixture contains indoxyl-3-phosphate, a substrate for ALP, and lucigenin (N,N'-dimethyl-9,9'-biacridinium dinitrate). ALP dephosphorylates indoxyl-3-phosphate to indol-3-ol, which subsequently undergoes oxidation. As a result, lucigenin is reduced to form a dioxetane structure that is cleaved to yield N-methylacridone. This compound produces a sustained luminescent glow following excitation. The raw relative luminescence units (RLUs) generated are measured by a photomultiplier tube in the FastPack® Analyzer and are directly proportional to the concentration of CRP in the sample. The entire reaction sequence takes place at 37 ± 0.5 °C and is protected from external light.

Intended Use

FastPack® High Sensitivity C-Reactive Protein Immunoassay is to be used for evaluation of conditions thought to be associated with inflammation, in otherwise healthy individuals. The FastPack® High Sensitivity C-Reactive Protein Immunoassay is intended for use with the FastPack® Analyzer. Not intended for Point-of-Care use.

FastPack® High Sensitivity C-Reactive Protein Calibrators are used for calibrating the quantitative FastPack® High Sensitivity C-Reactive Protein Immunoassay on the FastPack® Analyzer.

FastPack® High Sensitivity C-Reactive Protein Controls are used for quality control of the FastPack® High Sensitivity C-Reactive Protein Immunoassay on the FastPack® Analyzer.

FastPack® High Sensitivity C-Reactive Protein Verifiers are used in the quantitative verification of calibration and assay range of the quantitative FastPack® High Sensitivity C-Reactive Protein Immunoassay on the FastPack® Analyzer.

Comparison of new device to predicate devices

CHARACTERISTIC	Qualigen FastPack® High Sensitivity C-Reactive Protein Immunoassay	Olympus America, Inc. CRP Latex reagent K051564
Intended Use/ Indications for Use	FastPack® High Sensitivity C-Reactive Protein Immunoassay is to be used for evaluation of conditions thought to be associated with inflammation, in otherwise healthy individuals. The FastPack® High Sensitivity C-Reactive Protein Immunoassay is intended for use with the FastPack® Analyzer. Not intended for Point-of-Care use.	Olympus System Reagent and calibrators for the quantitative determination of C-Reactive Protein on OLYMPUS Analyzers. Measurement of CRP is useful for the detection and evaluation of infection, tissue injury, inflammatory disorders, and associated diseases. Measurements may also be used as an aid in the identification of individuals at risk of future cardiovascular disease. High sensitivity CRP (hsCRP) measurements, when used in conjunction with traditional clinical laboratory evaluation of acute coronary syndromes, may be useful as an independent marker of prognosis for recurrent events, in patients with stable coronary disease or acute coronary syndromes.
Sample Type	Serum or plasma (EDTA or lithium heparin)	Same
Sample Preparation	Standard processing for serum or plasma	Same
Interpretation of Results	Standard Curve	Same
Reagent Storage Temperature	2-8 ºC	Same
Testing Environment	Professional use	Same
Precision (% CV)	Within-run: ≤ 1.0% Between-run: ≤ 5.2% Total: ≤ 9.0%	Within-run: ≤ 3.2% Total: ≤ 3.8%
Linearity	Assay linear from 0.2 to 15.0 mg/L in High Sensitivity Application	Assay linear from 0.2 - 160 mg/L
Interfering Substances/Specificity	No interference from high levels of conjugated bilirubin, unconjugated bilirubin, hemoglobin, triglycerides, human serum albumin, L-ascorbic acid, oxaloacetic acid, glutathione, isoniazid, and L-DOPA; no interference from rheumatoid	No interference from high levels of bilirubin, hemoglobin, and triglycerides

	factor, human anti-mouse IgG, and transferrin	
Comparative Testing vs Established Methods	*FastPack® vs. Olympus AU2700* N = 131 Range of observations: 0.21 to 15.0 mg/L Deming regression: Slope (95% CI): 0.98 (0.95-1.02) y (95% CI): -0.12 (-0.23 to 0.00) R (95% CI) = 0.99 (0.99-0.99) Sy|x = 0.629	*AU400 vs. AU640* N = 109 Range of observations: 0.28-147.2 mg/L Deming regression: Slope = 1.025 y = -0.022 R = 0.999
Expected Values/Reference Intervals	0.2 - 11.4 mg/L	Cardiac risk assessment categories: Low < 1 mg/L Average 1.0 to 3.0 mg/L High > 3.0 mg/L

Differences between FastPack® and Olympus High-Sensitivity C-Reactive Protein Assays

CHARACTERISTIC	Qualigen FastPack® High-Sensitivity C-Reactive Protein Immunoassay	Olympus America, Inc. CRP Latex reagent K051564
Methodology	The FastPack® High Sensitivity C-Reactive Protein Immunoassay is a paramagnetic particle, chemiluminescent immunoassay employing specific monoclonal antibodies.	The Olympus CRP Latex reagent is a turbidimetric assay employing rabbit antibodies coated on latex particles.
Assay principle	Chemiluminescence	Turbidimetry
Assay procedure	Automated	Automated
Approximate assay time	8 minutes	3.5 minutes
Assay range	0.2 - 15.0 mg/L in High Sensitivity Application	0.2 - 160 mg/L (provides measurements both for "Normal Application" and "Highly Sensitive Application")
Traceability	Traceable to the ERM-DA474/IFCC reference which serves as the Primary Reference Material	"…traceable to an external standard." (K051564 510(k) Decision Summary)

Similarities between FastPack® and Olympus CRP Calibrators

CHARACTERISTIC	Qualigen FastPack® High-Sensitivity C-Reactive Protein Immunoassay	Olympus America, Inc. CRP Latex reagent K051564
Intended Use/Indication for Use	For in-vitro diagnostic use in calibrating FastPack® High-Sensitivity C-Reactive Protein Immunoassay	Olympus System Reagent and calibrators for the quantitative determination of C-Reactive Protein on Olympus Analyzers.
Antigen used in calibrators	Human CRP	Same
Matrix	Liquid human serum matrix containing a predetermined level of human CRP	Liquid human serum matrix containing predetermined levels of human CRP
Storage temperature	2-8 ºC	Same

Differences between FastPack® and Olympus CRP Calibrators

CHARACTERISTIC	Qualigen FastPack® High-Sensitivity C-Reactive Protein Immunoassay	Olympus America, Inc. CRP Latex reagent K051564
Number of calibrators	1	5 (additional calibrators provided at higher concentrations to enable CRP measurements in the "Normal Application")

Similarities between FastPack® and Predicate Controls

CHARACTERISTIC	Qualigen FastPack® High-Sensitivity C-Reactive Protein Immunoassay	Bio-Rad Laboratories Liquichek™ Cardiac Markers Plus Control K050537
Intended Use/Indication for Use	For in-vitro diagnostic use to monitor the precision and accuracy of the FastPack® High-Sensitivity C-Reactive Protein Immunoassay on the FastPack® Analyzer.	Liquichek™ Cardiac Markers Plus Control are intended for use as quality control serum to monitor the precision of laboratory testing procedures listing in the package insert.
Antigen used in controls	Human CRP	B-type Natriuretic Peptide, Creatine Kinase (Total), C-Reactive Protein, Homocysteine, Digitoxin, N-terminal pro-B-type Natriuretic Peptide, CK-MB, Myoglobin, Troponin I, Troponin T
Matrix	Liquid human serum matrix containing a predetermined level of human CRP	Prepared from human serum with added constituents of human and animal origin, preservatives, and stabilizers. The controls are in liquid form.
Storage temperature	2-8 ºC	2-8 ºC (Opened), or -20 to -70 ºC (Unopened)

Differences between FastPack® and Predicate Controls

CHARACTERISTIC	Qualigen FastPack® High-Sensitivity C-Reactive Protein Immunoassay	Bio-Rad Laboratories Liquichek™ Cardiac Markers Plus Control K050537
Number of levels	2	3

Similarities between FastPack® CRP Verifiers and Predicate Verifiers

CHARACTERISTIC	Qualigen FastPack® High-Sensitivity C-Reactive Protein Immunoassay	Ortho-Clinical Diagnostics, Inc. VITRO Chemistry Products hsCRP Performance Verifier, I, II, and III K041799
Intended Use/Indication for Use	For use in the quantitative verification of calibration and assay range of the quantitative FastPack® High-Sensitivity C-Reactive Protein Immunoassay on the FastPack® Analyzer.	VITROS hsCRP Performance Verifiers are assayed controls to monitor performance of hsCRP Reagent on VITROS 5,1 FS Chemistry Systems
Antigen used	Human CRP	Same
Storage temperature	2-8 ºC	Same
Matrix	Low Verifier: HEPES buffer with Bovine Serum Albumin (BSA) and Detergent (Cremophor A25) Mid and High Verifiers: Liquid human serum matrix containing a predetermined level of human CRP	A base matrix of human plasma proteins to which stabilizers and preservative have been added.
Number of levels	3	Same

Performance Summary

Precision

Precision was evaluated following the CLSI EP5-A2 guidance. Six serum patient samples with concentrations of ~0.5, 1.0, 2.0, 5.0, 7.5, and 12.5 mg/L CRP were tested in duplicate determinations in each of two runs per day on each of two FastPack® reagent lots, two FastPack® Analyzers per reagent lot, over a period of 20 days to yield 320 replicate determinations of each sample. A single FastPack® calibrator lot was utilized for all runs. Within-run, between-run, between-day, and residual components of variation were calculated as well as total imprecision using a general linear model. The table below presents the results:

		Within-Run		Between-Run		Between-Day		Residual		Total	
Sample	Overall Mean	SD	% CV	SD	% CV	SD	% CV	SD	% CV	SD	% CV
Serum Sample 1	0.38	0.002	0.53	0.014	3.68	0.005	1.32	0.029	7.74	0.033	8.68
Serum Sample 2	1.00	0.004	0.43	0.038	3.80	0.013	1.30	0.077	7.71	0.087	8.70
Serum Sample 3	2.06	0.008	0.39	0.071	3.45	0.030	1.46	0.162	7.89	0.180	8.74
Serum Sample 4	5.01	0.023	0.46	0.206	4.11	0.073	1.46	0.288	5.74	0.362	7.23
Serum Sample 5	7.67	0.035	0.46	0.314	4.09	0.111	1.45	0.596	7.78	0.684	8.92
Serum Sample 6	12.54	0.073	0.58	0.649	5.18	0.230	1.83	0.843	6.72	1.091	8.70

Limits of blank, detection, and quantitation

The Limit of Blank (LOB), the Limit of Detection (LOD), and the Limit of Quantitation (LOQ) of the FastPack® C-Reactive Protein Immunoassay were determined according to CLSI EP17-A: Protocols for Determination of Limits of Detection and Limits of Quantitation. The following are the limits determined:

LOB = 0.005 mg/L
LOD = 0.032 mg/L
LOQ = 0.063 mg/L

Linearity

Linearity was determined following CLSI EP6-A: Evaluation of the Linearity of Quantitative Measurement Procedures: a Statistical Approach: Approved Guideline. A high patient sample was intermixed with a low sample to generate 8 concentration levels each tested in triplicate determinations. Linear results were compared to 2nd and 3rd order polynomial fits against a pre-specified allowable error. The linearity range was found to extend from the LOQ (0.063 mg/L) to 15.0 mg/L. Samples recovering above the range may be diluted using Sample Diluent A.

Interferences

The following substances normally present in blood were tested and found not to interfere in the FastPack® High Sensitivity C-Reactive Protein Immunoassay at the noted concentrations:

Bilirubin (conjugated)	Tested to 40 mg/dL
Bilirubin (unconjugated)	Tested to 40 mg/dL
Hemoglobin	Tested to 750 mg/dL
Lipids	Tested to 1000 mg/dL

Human serum albumin	Tested to 7.7 g/dL
Transferrin	Tested to 567 mg/dL
Human IgG	Tested to 2961 µg/mL

The following exogenous substances potentially present in blood were tested and found not to interfere in the FastPack® High Sensitivity C-Reactive Protein Immunoassay at the noted concentrations:

L-ascorbic acid	Tested to 200 mg/dL
Oxaloacetic acid	Tested to 300 µM
Glutathione	Tested to 300 µM
Isoniazid	Tested to 300 µM
L-DOPA	Tested to 300 µM

Cross-reactivity

Rheumatoid factor at up to 1000 U/mL and human anti-mouse IgG at up to 4 µg/mL do not cross-react in the FastPack® High Sensitivity C-Reactive Protein Immunoassay. Additionally, heterophile samples with activity up to 3641 ng/mL do not interfere in the assay.

Serum and plasma equivalence

Blood collections were obtained from 41 volunteers and processed in parallel to serum, EDTA plasma, and lithium-heparin plasma. Measurements in FastPack® High Sensitivity C-Reactive Protein Immunoassay were compared via Deming regression and indicated equivalence between the three matrices.

Serum versus EDTA plasma

Parameter	Result
N compared	41
Range of observations, mg/L	Serum: 0.33 – 14.72 EDTA Plasma: 0.29 – 14.76
Absolute bias, mg/L	-0.225
% Bias	-6.1
Deming regression results	
Slope	0.94
y-intercept	0.0
R	0.984
R^2	0.967

Serum versus lithium-heparin plasma

Parameter	Result
N compared	41
Range of observations, mg/L	Serum: 0.33 – 14.72 Lithium-Heparin Plasma: 0.31 – 14.86
Absolute bias, mg/L	0.002
% Bias	0.5
Deming regression results	
Slope	1.00
y-intercept	0.00
R	0.993
R^2	0.986

Expected Values/Reference Intervals

A reference interval study employing serum samples from 211 subjects representing 4 different geographic regions of the United States yielded the results in the table below. The non-parametric 2.5^{th} - 97.5^{th} percentile of 0.2 - 11.4 mg/L provides the reference interval determined from this study.

Observed values	
Mean (SD)	3.2 (3.1) mg/L
Median (Min - Max)	1.9 (0.2 - 13.1) mg/L
2.5^{th} - 97.5^{th} percentile	0.2 - 11.4 mg/L

Newborns with no evidence of infection have CRP concentrations of < 2 mg/L (Soldin OP, Bierbower LH, Choi JJ, et al. Serum iron, ferritin, transferrin, total iron binding capacity, hs-CRP, LDL cholesterol and magnesium in children; new reference intervals using the Dade Dimension Clinical Chemistry System; Clin Chim Acta 2004;342:211-7.).

Method Comparison

Human serum samples were tested with the FastPack® High Sensitivity C-Reactive Protein Immunoassay and the obtained results were compared to the predicate method. A total of 131 samples ranging from 0.21 to 15.0 mg/L were tested in both assays. The FastPack® High Sensitivity C-Reactive Protein Immunoassay correlated well with the predicate method with correlation coefficient (R) of 0.99, slope = 0.98, and y-intercept = -0.12 mg/L.

Parameter	Result
Slope (95% CI)	0.98 (0.95-1.02)
y-intercept (95% CI)	-0.12 (-0.23 to 0.00)
R (95% CI)	0.99 (0.99 - 0.99)

SUMMARY

The information provided in this pre-market notification indicates that the FastPack® High Sensitivity C-Reactive Protein Immunoassay is substantially equivalent to the stated predicate device. The information further indicates that the FastPack® High Sensitivity C-Reactive Protein Immunoassay is safe and effective for its stated intended use.