DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
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July 14, 2017

ORTHO-CLINICAL DIAGNOSTICS, INC.
MARLENE HANNA, SENIOR MANAGER, REGULATORY AFFAIRS
100 INDIGO CREEK DRIVE
ROCHESTER, NY 14626

Re: K160712
Trade/Device Name: VITROS Chemistry Products hsCRP Reagent
Regulation Number: 21 CFR 866.5270
Regulation Name: C-reactive protein immunological test system
Regulatory Class: II
Product Code: DCK
Dated: June 9, 2017
Received: June 12, 2017

Dear Marlene Hanna:

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" (21CFR 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,

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: January 31, 2017
See PRA Statement below.

510(k) Number *(if known)*

K160712

Device Name
VITROS Chemistry Products hsCRP Reagent

Indications for Use *(Describe)*

VITROS Chemistry Products hsCRP Reagent:

For in vitro diagnostic use only. Rx Only.
VITROS Chemistry Products hsCRP Reagent is used on the VITROS 5,1 FS Chemistry System, the VITROS 4600 Chemistry System and the VITROS 5600 Integrated System to quantitatively measure C-reactive protein (CRP) in human serum and plasma. CRP is used to evaluate conditions thought to be associated with inflammation in otherwise healthy individuals.

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: k160712

VITROS Chemistry Products hsCRP Reagent: A summary of 510(k) safety and effectiveness information in accordance with the requirements of 21 CFR 807.92.

Submitter Information	
Name	Ortho-Clinical Diagnostics, Inc.
Address	100 Indigo Creek Drive Rochester, New York 14626
Phone number	585-453-4041
Fax number	585-453-3368
Establishment Registration	1319681
Name of contact person	Marlene Hanna
Date prepared	July 13, 2017
Trade or proprietary name	VITROS Chemistry Products hsCRP Reagent
Common or usual name	C-reactive protein immunological test system
Classification name	Cardiac c-reactive protein, antigen, antiserum
Classification panel	Immunology
Regulation	21 CFR 866.5270: C-Reactive Protein immunological test system Classification: Class II
Product Code(s)	DCK
Legally marketed device(s) to which equivalence is claimed	The Diazyme high sensitivity C-reactive protein (hsCRP) assay (k103557)
Device description	The quantitative measurement of C-reactive protein (CRP) is performed using the VITROS Chemistry Products hsCRP Reagent in conjunction with the VITROS Chemistry Products Calibrator Kit 17 and VITROS Chemistry Products FS Calibrator 1 on the VITROS 5,1 FS/4600 Chemistry System and the VITROS 5600 Integrated System. The VITROS Chemistry Products hsCRP Reagent is a dual chambered package containing ready-to-use liquid reagents. Samples, calibrators and controls are mixed with Reagent 1 containing a buffer. Addition of anti-CRP antibodies coupled to latex microparticles (Reagent 2) produces an immunochemical reaction yielding CRP antigen/antibody complexes. The turbidity is measured spectrophotometrically at 660 nm. Once a calibration has been performed for each reagent lot, the CRP concentration in each unknown sample can be determined using the stored calibration curve and the measured absorbance obtained in the assay of the sample.

Intended Use	**VITROS hsCRP Reagent:** For in vitro diagnostic use only. Rx ONLY. VITROS Chemistry Products hsCRP Reagent is used on the VITROS 5,1 FS Chemistry System, the VITROS 4600 Chemistry System and the VITROS 5600 Integrated System to quantitatively measure C-reactive protein (CRP) in human serum and plasma. CRP is used to evaluate conditions thought to be associated with inflammation in otherwise healthy individuals.

Comparison with Predicate Devices:

Table 1: VITROS Chemistry Products hsCRP Reagent

Characteristic	Predicate (Diazyme high sensitivity C-Reactive Protein: k103557)	New Device (VITROS hsCRP Reagent (Modified))
Intended Use	For in vitro diagnostic use only. Rx ONLY. The Diazyme high sensitivity C-reactive protein (hsCRP) assay is for the in vitro quantitative determination of C-reactive protein (CRP) in human serum and plasma on automated clinical chemistry analyzers. Measurement of CRP is of use for the detection and evaluation of inflammatory disorders and associated diseases, infection and tissue injury.	For in vitro diagnostic use only. Rx ONLY. VITROS Chemistry Products hsCRP Reagent is used to quantitatively measure C-reactive protein (CRP) in human serum and plasma. CRP is used to evaluate conditions thought to be associated with inflammation in otherwise healthy individuals.
Basic Principle	Latex enhanced immunoturbidimetric assay	Two-point rate, 2mmune-turbidimetric assay
Sample type	Serum, plasma	Serum, plasma
Assay Range Serum, Plasma	0.20 to 20.0 mg/L	0.34 to 15.00 mg/L

Performance Summary:

Substantial Equivalence was demonstrated by testing several performance characteristics including method comparison, precision, reference interval, linearity and detection limit.

Method Comparison:

Method Comparison testing followed CLSI Protocol EP09-A3, *Measurement Procedure Comparison and Bias Estimation Using Patient Samples. Approved Guideline - Third Edition.* A total of 119 human serum samples were tested. The 119 samples were measured with VITROS hsCRP assay on the VITROS 5600, 4600, and 5,1 Systems and a predicate method, Diazyme

hsCRP assay on the Hitachi 917 Systems. Of the 119 samples tested 113 were within the measuring range of both the VITROS hsCRP assay (0.34-15.0 mg/L) and the Diazyme hsCRP assay (0.20 – 20.0 mg/L).

The relationship between the VITROS hsCRP method and the Predicate method (Diazyme hsCRP) based on data from 113 samples on the VITROS 5600 Chemistry System is as follows:

VITROS 5600 Integrated System = 1.02 x Diazyme hsCRP Method + 0.26

The relationship between the VITROS hsCRP method on the VITROS 4600 System and the VITROS 5600 System based on data from 110 samples is as follows;

VITROS 4600 Integrated System = 1.02 x VITROS 5600 System + 0.01

The relationship between the VITROS hsCRP method on the VITROS 5,1 FS System and the VITROS 5600 System based on data from 109 samples is as follows;

VITROS 5,1 FS System = 1.07 x VITROS 5600 System + 0.11

The data demonstrates acceptable correlation was obtained between the VITROS hsCRP assay (traceable to European Reference Material ERM®-DA474/IFCC) versus the predicate method (traceable to European Reference Material ERM®-DA472/IFCC) and between VITROS Systems.

Precision:

The method was based upon the Clinical and Laboratory Standards Institute (CLSI) Protocol EP05-A3, *Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline-Third Edition, October 2014*. Five replicates of three human serum sample pools were run once per day for five days using two hsCRP Reagent lots and two Calibrator Kit 17 lots across three VITROS Chemistry Systems.

Testing was conducted using VITROS Chemistry Products hsCRP Reagent calibrated with VITROS Chemistry Products Calibrator Kit 17 and VITROS Chemistry Products FS Calibrator 1 traceable to ERM-DA474. Precision study results for the VITROS hsCRP assay are listed in table 1.

Table 1: Precision study

Analyzer	Reagent Lot	Mean Conc.	Within-run		Between-run		Total	
			SD	%CV	SD	%CV	SD	%CV
5,1 FS PM675	35-5544	0.96	0.067	6.96	0.000	0.00	0.067	6.96
		9.65	0.104	1.08	0.080	0.83	0.132	1.37
		13.41	0.156	1.16	0.081	0.60	0.176	1.31
	36-5726	1.02	0.060	5.90	0.024	2.36	0.065	6.39
		9.89	0.151	1.53	0.124	1.25	0.196	1.98
		13.86	0.266	1.92	0.134	0.97	0.298	2.15
4600 PM102	35-5544	0.97	0.063	6.53	0.000	0.00	0.063	6.53
		9.52	0.188	1.97	0.000	0.00	0.188	1.97
		13.12	0.269	2.05	0.067	0.51	0.277	2.11
	36-5726	1.01	0.047	4.66	0.021	2.08	0.052	5.16
		9.79	0.253	2.58	0.144	1.47	0.291	2.97
		13.64	0.400	2.93	0.078	0.57	0.408	2.99
5600 PM109	35-5544	0.92	0.053	5.77	0.000	0.00	0.053	5.77
		9.34	0.081	0.87	0.081	0.87	0.115	1.23
		12.78	0.126	0.99	0.110	0.86	0.167	1.31
	36-5726	1.00	0.054	5.40	0.000	0.00	0.054	5.40
		9.54	0.113	1.18	0.121	1.27	0.165	1.73
		13.26	0.278	2.10	0.148	1.12	0.315	2.38

Expected values/Reference range:

The reference interval was verified according to CLSI EP28-A3 *Defining, Establishing, and Verifying Reference Intervals in the Clinical Laboratory; Approved Guideline – Third Edition*; a 50% male and 50% female population was utilized. Reference intervals may differ for each population studied and therefore each laboratory should confirm the validity of these intervals for the population it serves. Increases in CRP values are non-specific and should be interpreted together with a complete clinical history. Follow-up testing of patients with elevated CRP values should be performed.

Conventional and SI Units (mg/L)
<5.0

Linearity:

Linearity was determined following CLSI EP6-A: *Evaluation of the Linearity of Quantitative Measurement Procedures: a Statistical Approach: Approved Guideline*. A high CRP serum pool was intermixed with a low serum pool to generate 13 concentration levels each tested in three replicate 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 across the measuring range of 0.34 to 15 mg/L.

Limits of blank, detection, and quantitation:

The Limit of Blank (LoB) for VITROS Chemistry Products hsCRP Reagent is 0.21 mg/L. The Limit of Detection (LOD) is 0.26 mg/L. The Limit of Quantitation (LOQ) is 0.34 mg/L. All results were determined according to the guidelines listed in CLSI EP17-A2 and the guidance for Industry and FDA Staff Review Criteria for Assessment of High Sensitivity C-Reactive Protein (hsCRP) issued September 22, 2005.

LoB*	**LoD****	**LoQ*****
0.21 mg/L	0.26 mg/L	0.34 mg/L

* Limit of Blank: The highest result to be reported for a blank sample with a 95% level of confidence ($\alpha = 0.05$).
** Limit of Detection: The amount of analyte where 95% of measurement results ($\beta = 0.05$) exceed the Limit of Blank.
*** Limit of Quantitation: The minimum amount of analyte that can be quantitatively determined based on acceptable precision.

Conclusion:

The conclusions drawn from the nonclinical tests (discussed above) demonstrate the modified VITROS Chemistry Products hsCRP Reagent is as safe, effective, and perform as well as the predicate device. The information submitted in the premarket notification is complete and supports a substantial equivalence decision.