K121558

SEP 21 2012

510(k) SUMMARY

Summary of 510(k) safety and effectiveness information is being submitted in accordance with the requirements of SMDA 1990 and 21 CFR 807.92

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Name of the Device:	Diazyme hsCRP POC Test Kit; Diazyme hsCRP POC Control Kit
Manufacturing Address	Diazyme Laboratories 12889 Gregg Court Poway, CA 92064 USA
Establishment Registration	2032900

Executive Summary

Detailed performance characteristics and comparison analysis are given in this filing that demonstrates substantial equivalence of the hsCRP POC Assay Kit to predicate device that is currently being marketed. The performance characteristics of the hsCRP POC Assay Kit are substantially similar to that of the approved predicate device (K103557). Performance data and risk analysis indicates that differences should not affect the safety and effectiveness of the hsCRP POC Assay and offers POL users an *in vitro* diagnostic device system to measure CRP in human venous whole blood samples.

Intended Use:

The Diazyme high sensitivity C-reactive protein (hsCRP) POC Test Kit is for the *in vitro* quantitative determination of C-reactive protein (CRP) in human venous whole blood on SMART 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.

The Diazyme hsCRP POC Control set is intended for use as quality controls for the Diazyme hsCRP POC Test Kit. For *in vitro* diagnostic use only.

Device Description:

Clinical Significance

CRP (C-reactive protein) is an acute phase protein whose concentration is seen to increase as a result of the inflammatory process, most notably in response to pneumococcal (bacterial) infectious, histolytic disease and a variety of disease states. Originally discovered by Tillet et al. in 1930 in patient sera with acute infection, CRP has now come to be used as a marker or general diagnostic indicator of infections and inflammation, in addition to serving as a monitor of patient response to therapy and surgery. Furthermore, regular measurements of CRP in infants can be a useful aid in the early diagnosis of infectious disease.

Assay Principle

Diazyme's hsCRP POC Test Kit is based on a latex enhanced immunoturbidimetric assay on Diazyme's SMART analyzer. Agglutination occurs when an antigen-antibody reaction occurs between CRP in a sample and anti-CRP which has been sensitized to latex particles. This agglutination is detected as an absorbance change (700 nm), with the magnitude of the change being proportional to the quantity of CRP in the sample. The instrument calculates the CRP concentration of patient specimen by use of a lot specific calibration curve that is stored in an RFID card provided with each hsCRP POC kit. The RFID card is inserted in the SMART analyzer and is needed for every single run.

Diazyme hsCRP POC Control Kit is intended for use as quality controls for the Diazyme hsCRP POC Test Kit and is packaged separately. The quality controls assist laboratory users in verification steps ensuring that the assay reagents are functioning correctly. QC materials are run exactly as samples. Users are instructed to verify the calibration curve with the controls and run controls each time a new lot of reagents are received. If QC materials fall outside laboratory acceptable range, users are instructed to re-test and call manufacturer customer service if problem persists.

SMART Analyzer (K092911) is a compact cuvette based spectrophotometer (10 inches x 5.5 inches x 5.5 inches) machine for point-of-care testing designed to analyze readings from single use reagent cuvette. The instrument only uses the Diazyme Reagent System (DRS) cuvette and caps and performs assay with a preprogrammed Radio Frequency ID (RFID) card. The DRS cuvette is supplied prefilled with Reagent 1 (R1) and the DRS cap is supplied prefilled with Re-

agent 2 (R2). The DRS cuvette and caps are kept separate until use. Users are instructed (see proposed labeling) to add 20µl of sample to the DRS cuvette prefilled with R1 containing proper amount of detergent for whole blood lysis. Users are then instructed to snap in place DRS cap and insert into analyzer. The instrument warms the cuvette to 37°C and after a predefined period adds the reagent R2 found in the DRS cap. The reagents and samples are mixed magnetically and absorbance readings are taken at 700nm. The lot specific RFID card contains reagent addition time, mixing time, reading time and calibration curve.

The Diazyme hsCRP POC Test Kit system thus consists of the following:

- hsCRP POC Test Kit. Reagents are provided in prefilled tubes, cuvettes and cuvette caps. The DRS cuvette and cuvette caps can only work with the SMART analyzer.
- hsCRP POC Control Kit. Controls are provided for quality control of the hsCRP POC Assay.

Equipment needed for Diazyme hsCRP POC Test Kit:

- SMART Analyzer (K092911).

Kit components (Candidate device)
Reagent 1 40 DRS cuvette (prefilled) • 100 mM TrisCl buffer
Reagent 2 40 DRS caps (prefilled) • Suspension of anti-human CRP polyclonal antibody coated latex particles (< 0.5%).
Calibrator
1 x preprogrammed lot specific RFID card in each kit
Control Set
1 x 1.0 mL Control 1
1 x 1.0 mL Control 2

Performance Testing Summaries:

Precision:

(1) Internal precision study performed at Diazyme Laboratories

The precision of the Diazyme hsCRP POC Test Kit was evaluated according to Clinical and Laboratory Standards Institute (CLSI) EP5-A guideline with the following modifications: In the study, three whole blood specimens containing 0.80 mg/L, 3.25 mg/L, and 12.50 mg/L CRP were tested in 4 runs per day over 10 days. Testing was performed on three different SMART Analyzers.

The mean value (Mean), standard deviation, within run imprecision and total imprecision CV mg/L are calculated and summarized in the following tables:

Within Run precision CV%

Total data points	Whole blood 1 0.80 mg/L hs-CRP 40	Whole blood2 3.25 mg/L hs-CRP 40	Whole blood 3 12.50 mg/L hs-CRP 40
Mean (mg/L)	0.813	3.186	12.560
SD	0.0782	0.0901	0.2247
CV	9.62%	2.83%	1.79%

Total Precision CV%

Total data points	Whole blood 1 1.00 mg/L hs-CRP 40	Whole blood2 3.25 mg/L hs-CRP 40	Whole blood 3 12.50 mg/L hs-CRP 40
Mean (mg/L)	0.813	3.186	12.560
SD (mg/L)	0.0664	0.0984	0.2667
CV mg/L	8.17%	3.09%	2.12%

(2) External precision study performed at POL sites

The precision was also evaluated at three (3) physician office laboratories (POL) by intended users such as nurses and office assistants. Six (6) whole blood samples containing C Reactive Protein levels ranging from low to high were used for the external precision study. At each site, 2 whole blood samples were tested. Each sample was run 4 times per day for 5 days using three SMART Analyzers.

The results are summarized in the following table:

Within Run

	Site 1		Site 2		Site 3	
	Whole blood 1	Whole blood 2	Whole blood 3	Whole blood 4	Whole blood 5	Whole blood 6
No. of Points	20	20	20	20	20	20
Mean (mg/L)	0.798	4.796	0.758	17.796	7.780	18.725
SD (mg/L)	0.0372	0.3369	0.0684	0.7447	0.4225	0.9409
CV	4.67%	7.02%	9.04%	4.18%	5.43%	5.02%

Total

	Site 1		Site 2		Site 3	
	Whole blood 1	Whole blood 2	Whole blood 3	Whole blood 4	Whole blood 5	Whole blood 6

No. of Points	20	20	20	20	20	20
Mean (mg/L)	0.798	4.796	0.758	17.796	7.780	18.752
SD (mg/L)	0.0684	0.3674	0.0616	0.7153	0.4082	0.8951
CV	8.58%	7.37%	8.13%	4.02%	5.24%	4.78%

Linearity
A set of eleven levels of linearity materials were prepared by diluting a whole blood sample containing 28.0 mg/L of C Reactive Protein (CRP) with a whole blood sample containing 0.47 mg/L CRP according to Clinical and Laboratory Standards Institute EP6-A and were tested with the Diazyme C Reactive Protein POC Test in triplicate on the SMART Analyzer. Linearity data and the LOQ data support Analytical Measuring Range (AMR) of 0.47 mg/L to 23.0 mg/L.

Limit of Detection
The LOB, LOD and LOQ of Diazyme hsCRP Assay were determined according to CLSI EP17-A: Protocols for Determination of Limits of Detection and Limits of Quantitation; Approved Guideline.

Results:
LOB is 0.055 mg/L
LOD is 0.15 mg/L
LOQ is 0.47 mg/L

Analytical specificity
Common endogenous substance interference

Protocol: Clinical and Laboratory Standards Institute EP7-A "Interference Testing in Clinical Chemistry": dose-response guidelines.

Acceptance criteria: < 10% deviation from samples without interferents.

The common interfering substances had no significant interference up to the concentrations summarized below.

Interference	Concentration
Triglyceride	1000 mg/dL
Ascorbic Acid	176 mg/dL
Bilirubin	40 mg/dL
Bilirubin Conjugated	30 mg/dL
Hemoglobin	20 g/dL
Rheumatoid Factor	250 IU/mL

Common exogenous substance interference

Protocol: Clinical and Laboratory Standards Institute EP7-A "Interference Testing in Clinical Chemistry": dose-response guidelines.

Acceptance criteria: < 10% deviation from samples without interferents.

The common interfering substances had no significant interference up to the concentrations summarized below.

Interference	Concentration
Oxaloacetate	200 µM
Glutathione	200 µM
Isoniazid	200 µM
L-DOPA	200 µM

Method comparison with predicate device:

Protocol: Clinical and Laboratory Standards Institute EP9-A2 - Method Comparison and Bias Estimation Using Patient Samples: Approved Guideline-Second Edition (2002).

Acceptance Criteria: Slope = 0.90~1.10; $r^2 \geq 0.95$

(1) Internal method comparison

A total of forty EDTA whole blood specimens were tested with Diazyme hsCRP POC Test on SMART analyzer. The correspondent plasma samples were tested with Diazyme hsCRP Assay on Hitachi 917 analyzer (predicate k103557).

The regression results are summarized in the following table:

	Whole blood application
n	40
Slope (w/ 95% Confidence Interval)	0.9871 (0.8122-1.0325)
Intercept (w/ 95% Confidence Interval)	-0.4004 (-0.2810 to 0.0540)
Correlation coefficient	0.9511
Range of values	0.47-22.50

(2) External method comparison

Method comparison was also performed at three (3) POL sites by intended users. One hundred and twenty (120) paired human whole blood-serum samples (a tube of venous whole blood and a tube of serum from the same individual) were tested for comparison.

At each site of the three sites, 40 whole blood samples were tested using SMART analyzers. The corresponding one hundred and twenty (120) plasma specimens were tested on Hitachi 917 with predicate device (k103557) at Diazyme Laboratories. One hundred and sixteen were used after excluding four samples that were out of the assay detection range.

The regression results are summarized in the following table:

	Site 1	Site 2	Site 3	3POL Site Combined
n	38	39	39	116
Slope (w/ 95% Confidence Interval)	0.9195 (0.8996 - 0.9927)	1.0125 (0.9508 - 1.0484)	1.0073 (0.9017 - 1.0369)	0.9712 (0.9420 - 1.0056)
Intercept (w/ 95% Confidence Interval)	0.0531 (-0.0395 - 0.1689)	-0.0839 (-0.1744 - 0.1349)	-0.2795 (-0.3237 - 0.0040)	-0.0870 (-0.0463 - 0.0686)
Correlation coefficient	0.9889	0.9811	0.9858	0.9836
Range of values	0.60-19.55	0.47-14.00	0.51-22.79	0.47-22.79

Expected value/Reference range

Previously established for predicate devices

To verify the transferability of the reference interval from the predicate device, whole blood samples from 150 apparently healthy individuals were tested using the Diazyme hsCRP POC Test according to CLSI C28-A3 guideline. The 150 whole blood samples were from apparently healthy male and female adults ≥ 18 years of age. The expected normal range is verified: < 5.0 mg/L in 95% of the population tested.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration

10903 New Hampshire Avenue
Silver Spring, MD 20993

Diazyme Laboratories
c/o Abhijit Datta
12889 Gregg Court
Poway, CA 92064

SEP 21 2012

Re: k121558
Trade Name: Diazyme high sensitivity C-reactive protein (hsCRP) POC Test kit and
Diazyme high sensitivity C-reactive protein (hsCRP) POC control kit
Regulation Number: 21 CFR §866.5270
Regulation Name: C-reactive protein immunological test system
Regulatory Class: Class II
Product Codes: DCK, JJX
Dated: August 7, 2012
Received: August 9, 2012

Dear Dr. Datta:

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.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to such additional controls. Existing major regulations affecting your device can be found in Title 21, Code of Federal Regulations (CFR), Parts 800 to 895. 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); and good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820).

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801), please contact the Office of In Vitro Diagnostic Device Evaluation and Safety at (301) 796-5450. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding postmarket surveillance, please contact CDRH's Office of Surveillance and Biometric's (OSB's) Division of Postmarket Surveillance at (301) 796-5760. 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 Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 796-5680 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm

Sincerely yours,

Courtney H. Lias, Ph.D.
Director
Division of Chemistry and Toxicology Devices
Office of *In Vitro* Diagnostic Device
Evaluation and Safety
Center for Devices and Radiological Health

Enclosure

Indications for Use

510(k) Number: K121558

Device Name: Diazyme high sensitivity C-reactive protein (hsCRP) POC Test kit and Diazyme high sensitivity C-reactive protein (hsCRP) POC control set.

Indications for Use:

The Diazyme high sensitivity C-reactive protein (hsCRP) POC Test Kit is for the *in vitro* quantitative determination of C-reactive protein (CRP) in human venous whole blood on SMART 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.

The Diazyme hsCRP POC control set is intended for use as quality controls for the Diazyme hsCRP POC Test Kit. For *in vitro* diagnostic use only.

Prescription Use X AND/Or Over-The-Counter Use _____
(Part 21 CFR 801 Subpart D) (21 CFR 801 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE; CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of In Vitro Diagnostic Device Evaluation and Safety (OIVD)

Division Sign-Off
Office of In Vitro Diagnostic Device
Evaluation and Safety

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