K071474

DEC 10 2008

MPO 510K SUMMARY

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

Submitter's Name: George M. Plummer
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P.O. Box 6101
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Date of Preparation: May 22, 2007

Name of Product(s): Dimension MPO Flex® reagent cartridge

FDA Classification Name(s): Myeloperoxidase, Immunoassay, System, Test (866.5600)

FDA Guidance Documents: None applicable

Predicate Device(s): PrognostiX CardioMPO™ Enzyme Immunoassay (K050029)

Device Description(s):

The MPO method is a one-step enzyme immunoassay based on the "sandwich" principle. The sample is incubated with chromium dioxide particles coated with monoclonal antibodies specific for MPO, and conjugate reagent (β-galactosidase labeled monoclonal antibodies specific for MPO). A particle/MPO/conjugate sandwich forms during the incubation period. Unbound conjugate is removed by magnetic separation and washing. The sandwich bound β-galactosidase is combined with the chromogenic substrate chlorophenol red-β-D-galactopyranoside (CPRG). Hydrolysis of CPRG releases a chromophore (CPR). The concentration of MPO present in the patient sample is directly proportional to the rate of color change due to formation of CPR measured at 577 nm.

Intended Use:

MPO Flex® reagent cartridge:

The MPO method is an *in vitro* diagnostic test for the quantitative measurement of myeloperoxidase (MPO) in human plasma on the Dimension® clinical chemistry system with the heterogeneous immunoassay module. Myeloperoxidase measurements may be used in conjunction with clinical history, ECG, and cardiac biomarkers to evaluate patients presenting with chest pain that are at risk for major adverse cardiac events, including myocardial infarction, need for revascularization, or death.

MPO Calibrator:

The MPO Calibrator is an *in vitro* diagnostic product intended to be used to calibrate the Myeloperoxidase (MPO) method on the Dimension® clinical chemistry system with the heterogeneous immunoassay module.

MPO Control:

The myeloperoxidase control is an *in vitro* diagnostic product intended for use as an assayed quality control product to monitor the performance of the Myeloperoxidase (MPO) method on the Dimension® clinical chemistry system with the heterogeneous immunoassay module.

Substantial Equivalence

A summary of the performance attributes of the Siemens Healthcare Diagnostics MPO Flex® reagent cartridge and the predicate PrognostiX CardioMPO™ Enzyme Immunoassay (K050029) is provided in the following charts.

Table of Similarities

Item	PrognostiX MPO	Dimension® MPO
Intended Use	The *Cardio*MPO™ Reagent Kit is an enzyme immunoassay intended for the quantitative determination of myeloperoxidase in human plasma, to be used in conjunction with clinical history, ECG and cardiac biomarkers to evaluate patients presenting with chest pain that are at risk for major adverse cardiac events, including myocardial infarction, need for revascularization, or death.	The MPO method is an *in vitro* diagnostic test for the quantitative measurement of myeloperoxidase (MPO) in human plasma on the Dimension® clinical chemistry system with the heterogeneous immunoassay module. Myeloperoxidase measurements may be used in conjunction with clinical history, ECG, and cardiac biomarkers to evaluate patients presenting with chest pain that are at risk for major adverse cardiac events, including myocardial infarction, need for revascularization, or death.
Assay Type	Sandwich enzyme immunoassay	Sandwich enzyme immunoassay
Reportable Range	13 to 5000 pmol/L	20 to 5000 pmol/L
Hook Effect	No high dose effect up to 800,000 pmol/L	No high dose effect up to 800,000 pmol/L
Clinical study results	Odds ratio increases from 1.0 to a max. of 3.3 across 4 quartiles	Odds ratio increases from 1.0 to a max. of 2.3 across 4 quartiles

Expected Values	≤ 539 pmol/L	20 - 633 pmol/L
Analytical Specificity	< 0.15% cross-reactivity at high and low MPO concentrations for the following: a-1 Antitrypsin (1250 nmol/L), C-reactive protein (550 nmol/L), Lysozyme (4500 nmol/L), Immunoglobin A (400 nmol/L), Elastase (2500 nmol/L), Lactoperoxidase (800 nmol/L), Lactoferrin 800 nmol/L), COX1 (900 nmol/L), COX2 (900 nmol/L), Thyroid peroxidase (600 nmol/L), Troponin I (2150 nmol/L)	< 0.15% cross-reactivity at high and low MPO concentrations for the following: a-1 Antitrypsin (1250 nmol/L), C-reactive protein (550 nmol/L), Lysozyme (4500 nmol/L), Immunoglobin A (400 nmol/L), Elastase (2500 nmol/L), Lactoperoxidase (800 nmol/L), Lactoferrin 800 nmol/L), COX1 (900 nmol/L), COX2 (900 nmol/L), Thyroid peroxidase (600 nmol/L), Troponin I (2150 nmol/L); < 0.4% cross-reactivity for Eosinophil Peroxidase (922 nmol/L)

Table of Differences

Item	PrognostiX MPO	Dimension® MPO
Antibody	PrognostiX polyclonal rabbit and goat monoclonal	Siemens Healthcare Diagnostics mouse monoclonal
Calibration Interval	Calibration curve using six levels updated for each run.	Calibration curve updated for each lot, using five levels every 30 days with the same reagent lot.
Sample Volume	5 uL	30 uL
Sample	Lithium Heparin Plasma	EDTA, Li or Na sodium heparin plasma
Controls	3 level; human MPO in lithium heparin plasma	2 level; human MPO in BSA

Method performance Summary:

Analytical Results

Method Comparison

A split, lithium heparin patient sample method comparison demonstrated good agreement between the Siemens Healthcare Diagnostics Dimension® MPO method and the predicate PrognostiX CardioMPO™ Enzyme Immunoassay.

PrognostiX Sample Range	Dimension® Sample Range	n	Slope	Intercept	Correlation Coefficient
154-4869	189-4678	139	1.03	91.8	0.88

The model equation for the Passing Bablok regression statistics is: [results for Dimension® MPO] = slope x [comparative method results] + intercept.

Plasma Study Results

Comparison of matched EDTA, sodium heparin and lithium heparin plasma samples were tested with the Dimension® MPO method. The following table summarizes the Passing Bablok regression from the study.

Comparative Specimen	Slope	Intercept	Correlation Coefficient	N
Lithium Heparin vs. EDTA	1.01	-19.3	0.997	59
Lithium Heparin vs. Sodium Heparin	0.96	-7.2	0.999	49

Reproducibility

Typical precision observed for the Dimension MPO method is summarized below:

		Repeatability		Within Lab	
Sample	Mean (ng/mL)	SD (ng/mL)	%CV	SD (ng/mL)	%CV
Siemens Healthcare Diagnostics Level 1 Control	428.4	16.3	3.8	20.4	4.8
Siemens Healthcare Diagnostics Level 2 Control	3643.7	121	3.3	131.6	3.6
EDTA Plasma Pool	494.1	10.9	2.2	17.2	3.5
Heparin Plasma Pool	1465	43.6	3	53.3	3.6

The reproducibility testing was conducted in accordance with the CLSI Approved Guideline for User Evaluation of Precision Performance of Clinical Chemistry Devices EP5-A2. For each test level, a single test from two independent cups was analyzed twice per day. The repeatability and within-lab standard deviations were calculated by the analysis of variance method.

Clinical Study Results

EDTA plasma samples were obtained from 400 patients who presented to the Emergency Department or acutely to out-patient facilities with chest pain or equivalent symptoms suggestive of ACS. Patients enrolled in the study were assessed for major adverse cardiac events (MACE) defined as myocardial infarction, revascularization (defined as coronary artery bypass graft, percutaneous coronary intervention, or placement of cardiac stent), or death. Incidence of MACE was assessed at 30 days and 6 months.

Logistic-regression models were used to calculate odds ratios and 95th percentile confidence

intervals. Odds ratios were calculated for MPO separately and after adjustment for age, gender, Troponin I, NT-proBNP, C-reactive protein, white blood cell count, ST-segment depression, history of hypertension, history of hypercholesterolemia, history of diabetes, and smoking status. The risk of MACE in all patients in the ensuing 30 day and 6 month period increased with increasing quartiles of myeloperoxidase concentration as shown in the following tables, demonstrating that MPO is an important predictor of MACE alone and in combination with other indicators of cardiovascular health.

MACE at 30 Days+

	Q1*	Q2	Q3	Q4
MPO (pmol/L)	94 – 581	582 – 894	895 – 1657	1658 – 5000
Odds Ratio	1.00	1.36	2.63	4.29
95% CI	NA	0.55 – 3.40	1.14 – 6.06	1.91 – 9.61
Adjusted Odds Ratio	1.00	1.41	3.03	4.31
95% CI	NA	0.51 – 3.89	1.19 – 7.76	1.62 – 11.50

MACE at 6 Months+

	Q1*	Q2	Q3	Q4
MPO (pmol/L)	94 – 581	582 – 894	895 – 1657	1658 – 5000
Odds Ratio	1.00	0.99	2.10	4.12
95% CI	NA	0.41 – 2.40	0.95 – 4.63	1.95 – 8.73
Adjusted Odds Ratio	1.00	0.98	2.21	3.66
95% CI	NA	0.37 – 2.56	0.93 – 5.26	1.50 – 8.94

+ The 95% CI's do not account for the random variation in the quartile values.
* In each analysis the first quartile served as the reference group for calculation of odds ratio

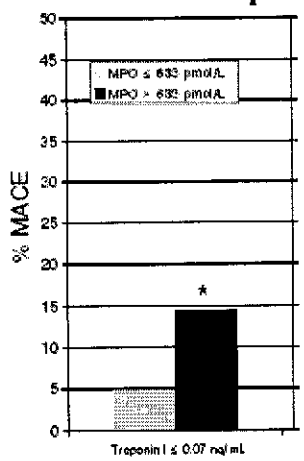
Logistic regression analysis was used to examine the added effect of MPO over various clinical and demographic covariates, one covariate at a time. A statistically significant effect of MPO was observed after separate adjustment for the effects of race, gender, hyperlipidemia and CRP. MPO did not have a statistically significant effect over troponin I.

ROC Curve Results for Predictive Probability of Covariates With and Without Addition of MPO			
Model†	0 days	30 days	180 days
Race	0.62	0.61	0.62
Race & MPO	0.72	0.71	0.71
Difference (95% CI)	-0.10 (-0.15 to -0.04)	-0.10 (-0.15 to -0.04)	-0.09 (-0.14 to -0.04)
p-value	0.0010	0.0011	0.0004
Sex	0.59	0.60	0.59
Sex & MPO	0.73	0.74	0.73
Difference (95% CI)	-0.14 (-0.21 to -0.07)	-0.14 (-0.20 to -0.08)	-0.14 (-0.20 to -0.08)
p-value	<0.0001	<0.0001	<0.0001
hsCRP	0.51	0.51	0.54
hsCRP & MPO	0.69	0.68	0.68
Difference (95% CI)	-0.17 (-0.26 to -0.09)	-0.17 (-0.26 to -0.08)	-0.14 (-0.22 to -0.06)
p-value	0.0001	0.0002	0.0003
Hyperlipidemia	0.63	0.64	0.62
Hyperlipidemia & MPO	0.73	0.73	0.71
Difference (95% CI)	-0.10 (-0.15 to -0.04)	-0.09 (-0.14 to -0.04)	-0.09 (-0.14 to -0.04)
p-value	0.0004	0.0003	0.0003

†Values for covariate and covariate plus MPO correspond to area under the ROC curve (AUC)

Further analysis of the clinical data was made by stratifying patients using the upper limit of the MPO reference interval (633 pmol/L) and Dimension Troponin I at the 99th percentile (0.07 ng/mL). The analysis shows that patients at risk for MACE within 30 and 180 days were identified significantly more often for MPO>633 pmol/L than for MPO 633 pmol/L when Troponin < 0.07 ng/mL.

MPO Provides Improved Stratification for MACE When Combined With Troponin I^{+}



* p = 0.008 vs. MPO ≤ 633 pmol/L. One sided p values were calculated using Fisher's Exact test

[+] Data shown represents incidence of MACE at 30 days; incidence of MACE at 180 days was similar

Comments on Substantial Equivalence:
Both the predicate PrognostiX MPO reagent cartridge and the Siemens Healthcare Diagnostics Dimension® MPO immunoassays are intended for the quantitative determination of myeloperoxidase. Comparative data for plasma samples demonstrate good analytical agreement between the methods. The clinical results with the Siemens Healthcare Diagnostics MPO assay demonstrates that Myeloperoxidase measurements may be used in conjunction with clinical history, ECG, and cardiac biomarkers to evaluate patients presenting with chest pain that are at risk for major adverse cardiac events, including myocardial infarction, need for revascularization, or death.

Conclusion:
The Siemens Healthcare Diagnostics Dimension® MPO and the predicate PrognostiX MPO immunoassays (K050029) are substantially equivalent based on their intended use and performance characteristics as described above.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

Siemens Healthcare Diagnostics
c/o Mr. George M. Plummer
Regulatory Affairs Director
P.O. Box 6101
Newark, DE 19714-6101

DEC 10 2008

Re: k071474
Trade Name: Dimension® MPO Flex® reagent cartridge, Dimension® MPO Calibrator, Dimension® MPO Control
Regulation Number: 21 CFR 866.5600
Regulation Name: Low-density lipoprotein immunological test system.
Regulatory Class: Class II
Product Codes: NTV, JIT, JJX
Dated: November 26, 2008
Received: December 02, 2008

Dear Mr. Plummer:

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); and good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820).

This letter will allow you to begin marketing your device as described in your Section 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific information about the application of labeling requirements to your device, or questions on the promotion and advertising of your device, please contact the Office of In Vitro Diagnostic Device Evaluation and Safety at (240) 276-0490. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). 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 (240) 276-3150 or at its Internet address at http://www.fda.gov/cdrh/industry/support/index.html.

Sincerely yours,

Jean M. Cooper, M.S., D.V.M.

Jean M. Cooper, M.S., D.V.M.
Director
Division of Chemistry and Toxicology
Office of *In Vitro* Diagnostic Device
Evaluation and Safety
Center for Devices and
Radiological Health

Enclosure

INDICATIONS FOR USE STATEMENT

510(k) Number (If Known): K071474

Device(s) Name(s):

Dimension® MPO Flex® reagent cartridge
Dimension® MPO Calibrator
Dimension® MPO Control

Indications for Use:

MPO Flex® reagent cartridge:

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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 Devices (OIVD)

Carol C Benson

...ion Sign-Off

Office of In Vitro Diagnostic Device
...luation and Safety

K071474