SUMMARY OF SAFETY AND EFFECTIVENESS

Assigned 510(k) Number

DEC 2 2 2006

The assigned 510(k) number is _____K063057_____.

Sponsor Name and Address

Diagnostic Products Corporation
Corporate Offices
5210 Pacific Concourse Drive
Los Angeles, CA
90045-6900
(310) 645-8200

Contact

Deborah L. Morris
Director, Clinical Affairs and Regulatory Submissions
(310) 645-8200 extension 7426
dmorris@dpconline.com

Device Name

Trade Name:	IMMULITE®/IMMULITE®1000, IMMULITE® 2000
Common Name:	High Sensitivity C-Reactive Protein
Classification	21 CFR 866.5270
Product Code	NQD
DPC Catalog Numbers:	LKCRP (100 tests), L2KCRP2 (200 tests), L2KCRP6 (600 tests)

Description of Device

The IMMULITE/IMMULITE 1000 and IMMULITE 2000 High Sensitivity CRP is a solid-phase, chemiluminescent immunometric assay. The assay utilizes a ¼-inch polystyrene bead coated with anti-ligand. The bead is co-incubated with sample, murine monoclonal anti-CRP, and alkaline phosphatase (bovine calf intestine)-conjugated to rabbit polyclonal anti-CRP in buffer for 30 minutes on each IMMULITE/IMMULITE 1000 and IMMULITE 2000 platform. Unbound enzyme conjugate is removed by a centrifugal wash procedure. Substrate is added and the resulting chemiluminescence is read in the luminometer.

Indications for Use

The IMMULITE®/IMMULITE® 1000 High Sensitivity CRP assay is intended for use as follows:

For *in vitro* diagnostic use with the IMMULITE/IMMULITE 1000 Analyzer — for the quantitative measurement of C-Reactive protein (CRP) in serum or plasma as an aid in the detection and evaluation of infection, tissue injury and inflammatory disorders, and associated diseases. Measurements may also be used as an aid in the identification of individuals at risk for future cardiovascular disease. High sensitivity CRP (hsCRP) measurements when used in conjunction with traditional clinical laboratory evaluation of acute coronary syndrome may be useful as an independent marker for recurrent events in patients with stable coronary disease or acute coronary syndrome.

IMMULITE® 2000 High Sensitivity CRP assay is intended for use as follows:

For *in vitro* diagnostic use with the IMMULITE 2000 Analyzer — for the quantitative measurement of C-Reactive protein (CRP) in serum or plasma as an aid in the detection and evaluation of infection, tissue injury and inflammatory disorders, and associated diseases. Measurements may also be used as an aid in the identification of individuals at risk for future cardiovascular disease. High sensitivity CRP (hsCRP) measurements when used in conjunction with traditional clinical laboratory evaluation of acute coronary syndrome may be useful as an independent marker for recurrent events in patients with stable coronary disease or acute coronary syndrome.

Manufacturing Site

IMMULITE®/IMMULITE® 1000 and IMMULITE 2000 High Sensitivity CRP assays are manufactured by Diagnostic Products Corporation at the following locations:

Diagnostic Products Corporation
Reagent Manufacturing Division
5700 West 96th Street
Los Angeles, CA 90045-5597
FDA Establishment #: 2017183

Diagnostic Products Corporation
Corporate Offices
5210 Pacific Concourse Drive
Los Angeles, CA 90045-6900
FDA Establishment #: 3005250747

Comparison to the Predicate

The IMMULITE/IMMULITE 1000 and IMMULITE 2000 High Sensitivity CRP assay reagents, components and all assay performance characteristics remain as previously established in 510(k) K003372.

A summary of the features of the IMMULITE/IMMULITE 1000 and IMMULITE 2000 High Sensitivity CRP assay and the predicate device, Dade Behring N *High Sensitivity* CRP, (K991385/K033908) is presented below.

Item	IMMULITE/IMMULITE 1000 and IMMULITE 2000 High Sensitivity CRP	Dade Behring N *High Sensitivity* CRP using BN™ Systems
Assay Type	Chemiluminescent immunometric	Particle enhanced immunoephelometry
Antibody	Anti-CRP Murine monoclonal and rabbit polyclonal anti-CRP	Mouse monoclonal Anti-CRP
Expected Values	Expected high sensitivity CRP values for healthy individuals has been established in the literature as <3 mg/L. A study performed on 100 apparently healthy volunteers yielded a median of 1.4 mg/L and an upper 97.5th percentile of 11 mg/L. The AHA/CDC Scientific Statement concerning inflammation and cardiovascular markers reports that hsCRP values < 1 mg/L are low risk for cardiovascular disease prediction; values between 1–3 mg/L are average risk for cardiovascular disease prediction; and values > 3 mg/L are high risk for cardiovascular disease prediction. Increases in CRP are non-specific and should not be interpreted without a complete clinical history. Consider these limits as guidelines only. Each laboratory should establish its own reference ranges.	Expected values for healthy individuals as noted in the literature is <3 mg/L. The normal range of CRP in the serum of 2147 apparently healthy individuals using the CardioPhase hsCRP Assay was found to be 90% 1.69 mg/L 95% 2.87 mg/L A subset of the Stanisless Cohort was examined in this study. The cohort subset used consisted of 1151 males and 996 females ranging in age from 5 to 71 years. All participants were of European ancestry and free of previously diagnosed serious or chronic disease (such as cancer or cardiovascular disease) and excluded individuals taking anti-inflammatory drugs or antibiotics. As CRP is a nonspecific indicator for a wide range of disease processes, and as the reference individuals are affected by many factors that may differ for each population studied, each laboratory should determine its own reference interval.
Reference standards	WHO IS 85/506 and CRM 470	CRM 470
Indications for Use	For *in vitro* diagnostic use with the IMMULITE/IMMULITE 1000 and IMMULITE 2000 Analyzers — for the quantitative measurement of C-Reactive protein (CRP) in serum or plasma as an aid in the detection and evaluation of infection, tissue injury and inflammatory disorders and associated diseases. Measurements may also be used as an aid in the identification of individuals at risk for future cardiovascular disease. High sensitivity CRP (hsCRP) measurements when used in conjunction with traditional clinical laboratory evaluation of acute coronary syndrome may be useful as an independent marker for recurrent events in patients with stable coronary disease or acute coronary syndrome.	N *High Sensitivity* CRP is an in vitro diagnostic reagent for the quantitative determination of C-reactive protein (CRP) in human serum, and heparin and EDTA plasma by means of particle enhanced immunoephelometry using the BN Systems. In acute phase response, increased levels of a number of plasma proteins, including C-reactive protein is observed. 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 for future cardiovascular disease. High sensitivity CRP (hsCRP) measurements when used in conjunction

Item	IMMULITE/IMMULITE 1000 and IMMULITE 2000 High Sensitivity CRP	Dade Behring N *High Sensitivity* CRP using BN™ Systems
		with traditional clinical laboratory evaluation of acute coronary syndromes may be useful as an independent marker for recurrent events in patients with stable coronary disease or acute coronary syndromes.
Working Range	IMMULITE/IMMULITE 1000: 0.3 to 100 mg/L IMMULITE 2000: 0.2 to 100 mg/L	0.175 to 1100 mg/L
Analytic Sensitivity	IMMULITE/IMMULITE 1000: 0.1 mg/L IMMULITE 2000: 0.1 mg/L	0.175 mg/L
Functional Sensitivity	IMMULITE/IMMULITE 1000: 0.3 mg/L IMMULITE 2000: 0.2mg/L	Not reported in the package insert
Sample Type	Serum and Heparinized plasma	Serum, heparinized, and EDTA plasma
Interferences	No significant interference from conjugated bilirubin (up to 200 mg/L), hemoglobin (up to 570 mg/dL for IMMULITE/IMMULITE 1000, and 512 mg/dL for IMMULITE 2000), or triglycerides (up to 3000 mg/dL). No cross-reactivity with human serum albumin, human IgG, or transferrin	No significant interference from bilirubin (up to 230 mg/L), hemoglobin (up to 36 g/L) or triglycerides (up to 7.4 g/L).
Hook Effect	IMMULITE/IMMULITE 1000: No high dose hook effect up to 3780 mg/L IMMULITE 2000: No high dose hook effect up to 3780 mg/L	Not reported in the package insert.
Calibration Interval	Recommended 2 week adjustment interval	Reference curve valid for 4 weeks and beyond as indicated by control results

Standards/Guidance Documents Referenced

Guidance for Industry and FDA Staff: "Review Criteria for Assessment of C-Reactive Protein (CRP), High Sensitivity C-Reactive Protein (hsCRP) and Cardiac C-Reactive Protein cCRP Assays", issued September 22, 2005.

Clinical Laboratory Standard Institute (CLSI). *Protocols for the Determination of Limits of Detection and Limits of Quantitation*; Approved Guideline. CLSI document EP17-A Vol 24 No 34. CLSI 940 West Valley Road, Suite 1400, Wayne, Pennsylvania 19087-1898 USA, 2004.

Clinical Laboratory Standard Institute (CLSI). *Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline – Second Edition.* CLSI document EP5-A2. CLSI, 940 West Valley Road, Suite 1400, Wayne, Pennsylvania 19087-1898 USA, 2004.

Working Range

The IMMULITE/IMMULITE 1000 High Sensitivity CRP reportable range is 0.3 to 100 mg/L and the IMMULITE 2000 High Sensitivity CRP reportable range is 0.2 to 100 mg/L.

Standardization

The IMMULITE/IMMULITE 1000 and IMMULITE 2000 High Sensitivity CRP assays are standardized to both the WHO IS 85/506 and CRM 470 reference standards.

Analytical Sensitivity

The IMMULITE/IMMULITE 1000 and IMMULITE 2000 High Sensitivity CRP assays' analytical sensitivity is 0.1 mg/L as previously reported and cleared in Pre-market Notification 510(k) K003372 for IMMULITE/IMMULITE 1000 and IMMULITE 2000 hsCRP.

Functional Sensitivity

The IMMULITE/IMMULITE 1000 High Sensitivity CRP assay's functional sensitivity (lowest concentration that can be measured with a total CV% of 10%) is 0.3 mg/L.

The IMMULITE 2000 High Sensitivity CRP assay's functional sensitivity (lowest concentration that can be measured with a total CV% of 10%) is 0.2 mg/L.

Precision

As previously reported and cleared in Pre-market Notification 510(k) K003372 IMMULITE/IMMULITE 1000 High Sensitivity CRP intra- and inter-assay CV% were not greater than 7.5% at 0.8 mg/L, 6% at 1.5 mg/L, 4.8% at 3.1 mg/L, and 4.9% at 15.0 mg/L. Intra-assay CV% did not exceed 6.0% for all samples tested over the range 0.3 mg/L to 78 mg/L. Inter-assay CV% did not exceed 10% for all samples tested over the range 0.3 mg/L to 78 mg/L.

As previously reported and cleared in Pre-market Notification 510(k) K003372 IMMULITE 2000 High Sensitivity CRP intra- and inter-assay CV% were not greater than 7.1% at 0.85 mg/L, 3.1% at 3.2 mg/L, and 3.3% at 12.3 mg/L. Intra-assay CV% did not exceed 8.7% for all samples tested over the range 0.23 mg/L to 93.7 mg/L. Inter-assay CV% did not exceed 8.7% for all samples tested over the range 0.23 mg/L to 93.7 mg/L.

Linearity

The IMMULITE/IMMULITE 1000 and IMMULITE 2000 High Sensitivity CRP assays demonstrate linearity of dilution within the precision of the assay as previously reported and cleared in Pre-market Notification 510(k) K003372 for IMMULITE/IMMULITE 1000 and IMMULITE 2000 hsCRP .

Spiked Recovery

The IMMULITE/IMMULITE 1000 and IMMULITE 2000 High Sensitivity CRP assays demonstrate accuracy of spiked recovery within the precision of the assay as previously reported and cleared in Pre-market Notification 510(k) K003372 for IMMULITE/IMMULITE 1000 and IMMULITE 2000 hsCRP.

Interfering substances

The IMMULITE/IMMULITE 1000 and IMMULITE 2000 High Sensitivity CRP assays demonstrate that presence of conjugated bilirubin in concentrations up to 200 mg/L has no effect on results within the precision of the assay as previously reported and cleared in Pre-market Notification 510(k) K003372 for IMMULITE/IMMULITE 1000 and IMMULITE 2000 hsCRP.

The IMMULITE/IMMULITE 1000 and IMMULITE 2000 High Sensitivity CRP assays demonstrate that presence of hemoglobin in concentrations up to 570 mg/L on IMMULITE/IMMULITE 1000 and 512 mg/L on IMMULITE 2000 has no effect on results within the precision of the assay as previously reported and cleared in Pre-market Notification 510(k) K003372 for the IMMULITE/IMMULITE 1000 and IMMULITE 2000 hsCRP.

The IMMULITE/IMMULITE 1000 and IMMULITE 2000 High Sensitivity CRP assays demonstrate that presence of triglycerides in concentrations up to 3,000 mg/L has no effect on results within the precision of the assay as previously reported and cleared in Pre-market Notification 510(k) K003372 for the IMMULITE/IMMULITE 1000 and IMMULITE 2000 hsCRP.

Cross-Reactivity

The IMMULITE/IMMULITE 1000 and IMMULITE 2000 High Sensitivity CRP assays demonstrate no cross-reactivity to human serum albumin (HSA) at levels up to 1,000 mg/dL added HSA, human IgG at 1,000 mg/dL added IgG or transferrin at 1,000 mg/dL added tranferrin as previously reported and cleared in Pre-market Notification 510(k) K003372 for the IMMULITE/IMMULITE 1000 and IMMULITE 2000 hsCRP.

High Dose Hook Effect

The IMMULITE/IMMULITE 1000 and IMMULITE 2000 High Sensitivity CRP assays demonstrate no high dose hook effect up to 3780 mg/L.

Expected Values

Expected high sensitivity CRP values for healthy individuals has been established in the literature as <3 mg/L.

A study performed on 100 apparently healthy volunteers yielded a median of 1.4 mg/L and an upper 97.5th percentile of 11 mg/L.

The AHA/CDC Scientific Statement concerning inflammation and cardiovascular markers reports that hsCRP values < 1 mg/L are low risk for cardiovascular disease prediction; values between 1–3 mg/L are average risk for cardiovascular disease prediction; and values > 3 mg/L are high risk for cardiovascular disease prediction.

Increases in CRP are non-specific and should not be interpreted without a complete clinical history..

Consider these limits as guidelines only. Each laboratory should establish its own reference ranges.

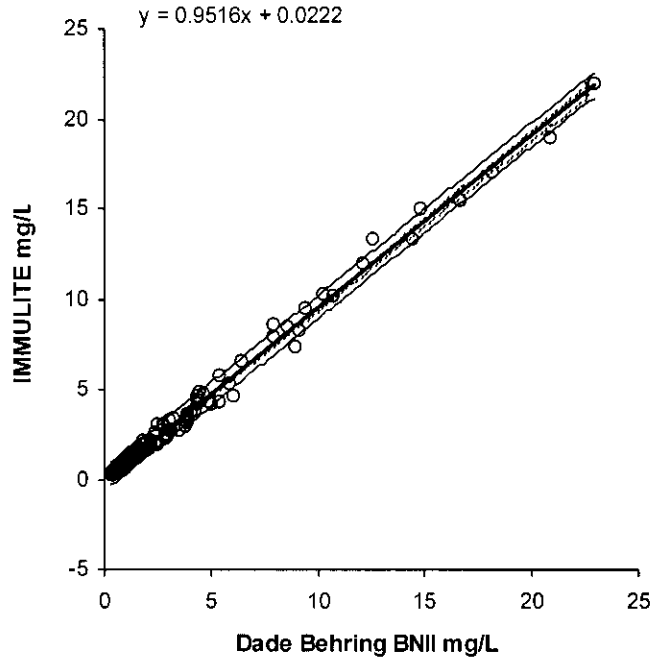
Comparison of IMMULITE/IMMULITE 1000 and IMMULITE 2000 hsCRP Results to the Predicate Dade Behring N High Sensitivity CRP

IMMULITE/IMMULITE 1000 HSCRP VERSUS DADE BEHRING N HSCRP

The IMMULITE/IMMULITE 1000 High Sensitivity CRP assay was compared to the Dade Behring N *High Sensitivity* CRP assay.

By linear regression (N=175, range 0.3 to 22.9 mg/L by Dade Behring, slope = 0.952 95%CI 0.939 to 0.965, intercept = 0.022 95%CI –0.0372 to 0.0817)
Mean Dade Behring: 2.7 mg/L
Mean IMMULITE: 2.6 mg/L

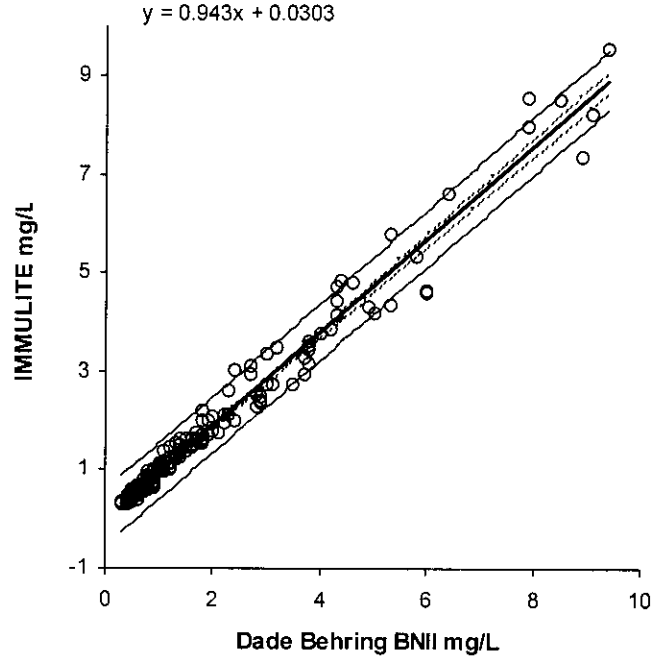
IMMULITE/IMMULITE 1000= 0.952 Dade Behring + 0.022 mg/L; r = 0.996



Using the same data set in the range no greater than 10 mg/L, by linear regression (N=165, range 0.3 to 9.4 mg/L by Dade Behring, slope = 0.943 95%CI 0.9195 to 0.9665, intercept = 0.0303 95%CI –0.0327 to 0.0933)

Mean Dade Behring: 1.9 mg/L
Mean IMMULITE: 1.8 mg/L

IMMULITE/IMMULITE 1000= 0.943 Dade Behring + 0.030 mg/L; r = 0.987

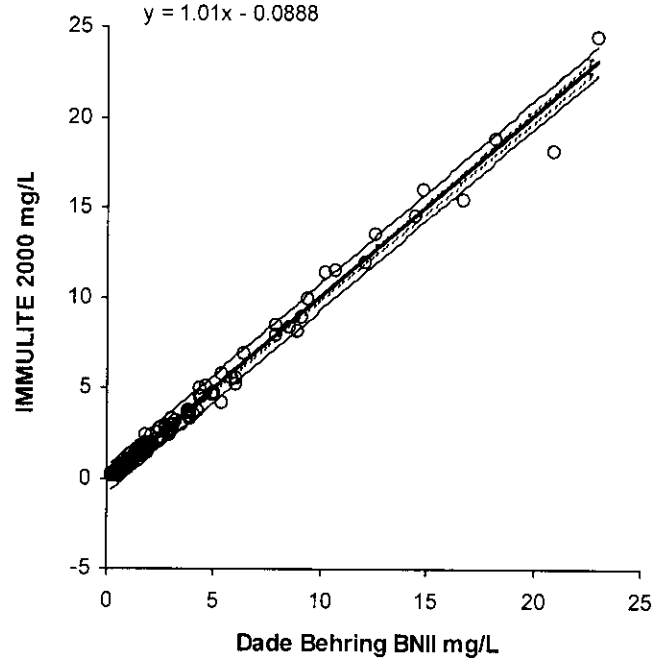


IMMULITE 2000 HSCRP VERSUS DADE BEHRING N HSCRP

The IMMULITE 2000 High Sensitivity CRP assay was compared to the Dade Behring N *High Sensitivity* CRP assay.

By linear regression (N=185, range 0.2 to 22.9 mg/L by Dade Behring, slope = 1.010 95%CI 0.9954 to 1.0246, intercept = -0.0888 95% CI –0.1542 to –0.0235)
Mean Dade Behring: 2.6 mg/L
Mean IMMULITE 2000: 2.5 mg/L

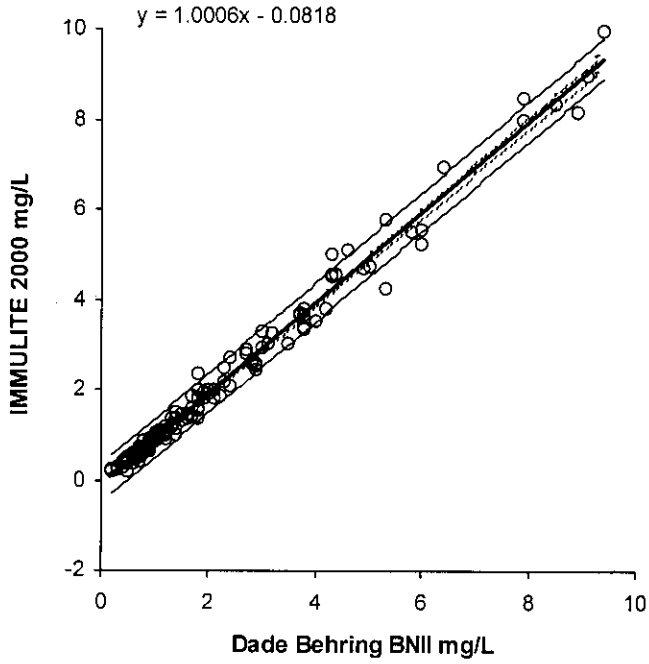
IMMULITE 2000 = 1.01 Dade Behring - 0 .0888 mg/L; r = 0.995



Using the same data set in the range no greater than 10 mg/L by linear regression (N=175, range 0.2 to 9.4 mg/L by Dade Behring, slope = 1.0006 95%CI 0.9833 to 1.0179, intercept = -0.0818 95%CI –0.1270 to –0.0367)

Mean Dade Behring: 1.8 mg/L
Mean IMMULITE: 1.7 mg/L

IMMULITE 2000 = 1.0006 Dade Behring - 0.0818 mg/L; r = 0.993



Conclusions

The IMMULITE/IMMULITE 1000 and IMMULITE 2000 hsCRP assays demonstrate substantial equivalence to the Dade Behring N *High Sensitivity* CRP assay.

The IMMULITE/IMMULITE 1000 and IMMULITE 2000 hsCRP assays are thereby safe and effective for the following intended use:

> The IMMULITE®/IMMULITE® 1000 High Sensitivity CRP assay is intended for *in vitro* diagnostic use with the IMMULITE/IMMULITE 1000 Analyzer — for the quantitative measurement of C-Reactive protein (CRP) in serum or plasma as an aid in the detection and evaluation of infection, tissue injury and inflammatory disorders, and associated diseases. Measurements may also be used as an aid in the identification of individuals at risk for future cardiovascular disease. High sensitivity CRP (hsCRP) measurements when used in conjunction with traditional clinical laboratory evaluation of acute coronary syndrome may be useful as an independent marker for recurrent events in patients with stable coronary disease or acute coronary syndrome.
>
> IMMULITE® 2000 High Sensitivity CRP assay is intended for *in vitro* diagnostic use with the IMMULITE 2000 Analyzer — for the quantitative measurement of C-Reactive protein (CRP) in serum or plasma as an aid in the detection and evaluation of infection, tissue injury and inflammatory disorders, and associated diseases. Measurements may also be used as an aid in the identification of individuals at risk for future cardiovascular disease. High sensitivity CRP (hsCRP) measurements when used in conjunction with traditional clinical laboratory evaluation of acute coronary syndrome may be useful as an

independent marker for recurrent events in patients with stable coronary disease or acute coronary syndrome.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

Deborah L. Morris
Director, Clinical Affairs and Regulatory Submissions
Diagnostic Products Corporation
Corporate Offices
5210 Pacific Concourse Drive
Los Angeles CA 90045-6900

DEC 2 2 2006

Re: k063057

Trade/Device Name: Immulite®/ Immulite® 1000 High Sensitivity CRP
Immulite® 2000 High Sensitivity CRP
Regulation Number: 21 CFR 866.5270
Regulation Name: C-reactive protein immunological test system
Regulatory Class: Class II
Product Code: NQD
Dated: September 15, 2006
Received: October 5, 2006

Dear Ms. Deborah L. Morris:

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

510(k) Number (if known): K063057

Device Name: IMMULITE®/IMMULITE® 1000 High Sensitivity CRP
IMMULITE® 2000 High Sensitivity CRP

Indications For Use:

The IMMULITE®/IMMULITE® 1000 High Sensitivity CRP assay is intended for use as follows:

For *in vitro* diagnostic use with the IMMULITE/IMMULITE 1000 Analyzer — for the quantitative measurement of C-Reactive protein (CRP) in serum or plasma as an aid in the detection and evaluation of infection, tissue injury and inflammatory disorders, and associated diseases. Measurements may also be used as an aid in the identification of individuals at risk for future cardiovascular disease. High sensitivity CRP (hsCRP) measurements when used in conjunction with traditional clinical laboratory evaluation of acute coronary syndrome may be useful as an independent marker for recurrent events in patients with stable coronary disease or acute coronary syndrome.

MMULITE® 2000 High Sensitivity CRP assay is intended for use as follows:

For *in vitro* diagnostic use with the IMMULITE 2000 Analyzer — for the quantitative measurement of C-Reactive protein (CRP) in serum or plasma as an aid in the detection and evaluation of infection, tissue injury and inflammatory disorders, and associated diseases. Measurements may also be used as an aid in the identification of individuals at risk for future cardiovascular disease. High sensitivity CRP (hsCRP) measurements when used in conjunction with traditional clinical laboratory evaluation of acute coronary syndrome may be useful as an independent marker for recurrent events in patients with stable coronary disease or acute coronary syndrome.

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

...on Sign-Off

Office of In Vitro Diagnostic Device
Evaluation and Safety

K063057