Bayer Diagnostics
ADVIA Centaur BNP Assay

Summary of Safety and Effectiveness

This Summary of Safety and Effectiveness has been prepared in accordance with the requirements of 21 CFR 807.92, to provide sufficient information to understand the basis for a determination of substantial equivalence.

1. Submitter Information

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Date Summary Prepared: March 28, 2003

2. Device Information

Propriety Name: ADVIA Centaur® B-Type Natriuretic Peptide (BNP) Assay

Common Name: BNP assay

Classification Name: B-type natriuretic peptide test system
Class: II
CFR: 21 CFR 862.1117
Product Code: NBC, JIT, JJX

3. Predicate Device Information

Name: Triage BNP Test

Manufacturer:
Manufactured by: Biosite Diagnostics Incorporated
11030 Roselle Street
San Diego, California 92121, USA

510(k) Number: K003475/K010266

4. Device Description

The ADVIA® Centaur® BNP assay is a fully automated two-site sandwich immunoassay using direct chemiluminescent technology, which uses constant amounts of two monoclonal antibodies. The first antibody, in the Lite Reagent, is an acridinium ester labeled monoclonal mouse anti-human BNP $F(ab')_2$ fragment specific to the ring structure of BNP. The second antibody, in the Solid Phase, is a biotinylated monoclonal mouse anti-human antibody specific to the C-terminal portion of BNP, which is coupled to streptavidin magnetic particles. Patient sample (calibrator or control materials) is incubated for 5 minutes at 37°C with the Lite Reagent that contains the tracer antibody conjugate. Subsequently, Solid Phase reagent is added and incubated for 2.5 minutes at 37°C. An immuno-complex is formed between the BNP in the sample and the two antibody conjugates. Following incubation, the unbound antibody conjugates are washed away. The chemiluminescence of the immuno-complex signal is measured in a luminometer. Samples with low BNP levels will have a minimum amount of bound AE label, while samples with high levels of BNP will have maximum label complex bound. Thus, a direct relationship exists between the amount of BNP present in the patient sample and the amount of relative light units (RLUs) detected by the system.

5. Statement of Intended Use

The Bayer ADVIA® Centaur® BNP assay is an *in vitro* immunoassay for the quantitative determination of B-type Natriuretic Peptide (BNP) in human plasma using the ADVIA® Centaur® System. This assay is indicated for the measurement of plasma BNP as an aid in the diagnosis of heart failure.

6. Substantial Equivalence

The Bayer ADVIA Centaur BNP assay is substantially equivalent to other devices legally marketed in the United States. The ADVIA Centaur BNP assay is similar to the Biosite Triage BNP predicate device cleared under K010266. Both products are two-site immunoassays, which are intended for use in the quantitative determination of the B-type Natriuretic Peptide.

(a) Technological Characteristics

The following table compares the technology features of the Bayer ADVIA Centaur BNP assay with the Biosite Triage BNP predicate device:

Feature	Bayer ADVIA Centaur® BNP Immunoassay	Biosite Triage® BNP Test (Predicate Device)
Intended Use	Quantitative determination of B-type Natriuretic Peptide	Measurement of B-type Natriuretic Peptide
Indication for Use	An aid in the diagnosis of heart failure.	An aid in the diagnosis of congestive heart failure.
Assay Principle	Chemiluminescence immunoassay	Fluorescence immunoassay
Traceability/Standardization	• Reference standard – synthetic human BNP (amino acid 77 to 108) in buffer based matrix.	Purified protein preparation of BNP based on the mass (concentration) of analyte present in EDTA plasma.

Feature	Bayer ADVIA Centaur® BNP Immunoassay	Biosite Triage® BNP Test (Predicate Device)
Calibration Interval	• After 28 days when using the same reagent lot • With every new primary reagent lot	Each kit
Sample Type	Human plasma using EDTA as anticoagulant	Human whole blood and plasma using EDTA as anticoagulant
Sample Volume	100 µL	~200 µL
Calibrator	BNP Calibrator set (2 levels)	Electronic code chip
Controls	BNP 1,2,3 Quality Control set	Triage® BNP Controls
Reagent Stability	Unopened • Until the expiration date when stored at 2-8°C Onboard • 41.6 days (or 60 days with the use of version 3.0 software or higher)	• Until the expiration date when stored at 2-8°C • 14 days at room temperature
Instrument	ADVIA Centaur System, a fully automated, random-access immunoassay analyzer	Triage® Meter
Measuring Range	<2.0 – 5000 pg/mL	5 – 5000 pg/mL

(b) Performance Characteristics

The following table compares the performance characteristics of the Bayer ADVIA Centaur BNP assay with the Biosite Triage BNP predicate device:

Feature	Bayer ADVIA Centaur® BNP Immunoassay	Biosite Triage® BNP Test (Predicate Device)
Expected Values	• Age and gender-matched descriptive statistics provided • Decision threshold of 100 pg/mL recommended	• Age and gender-matched descriptive statistics provided • Decision threshold of 100 pg/mL recommended
Precision	• Within-run 1.8 – 4.3 %CV from 29.4 – 1736.0 pg/mL • Total 2.3 – 4.7 %CV from 29.4 – 1736.0 pg/mL	• Average within-day 9.4 – 15.2 %CV from 28.8 – 1080.4 pg/mL • Average total 10.1 – 16.2 % CV from 28.8 – 1080.4 pg/mL
Hook Effect	No high dose effect up to 100,000 pg/mL	N/A
Analytical Sensitivity	<2 pg/mL	5 pg/mL
Dilution Recovery	On-board dilution 1:2, 1:5 and 1:10 with average recovery of 97%.	No sample dilution. For patient samples with BNP levels higher than the measurable range of the Triage BNP Test (>5000 pg/mL), the test should be interpreted as having a positive result because the BNP concentration is significantly elevated.
Limitations/Warning/Precautions	• This test has been evaluated with plasma using EDTA as the anticoagulant. Serum,	• This test has been evaluated with whole blood and plasma using EDTA as the

Feature	Bayer ADVIA Centaur® BNP Immunoassay	Biosite Triage® BNP Test (Predicate Device)
	sodium citrate, lithium heparin and sodium fluoride sample tubes have also been tested and are not recommended. • No interference from hemoglobin up to 1000 mg/dL • No interference from triglycerides up to 800 mg/dL • No interference from cholesterol up to 1000 mg/dL • No interference from urea up to 200 mg/dL • No interference from creatinine up to 2.5 mg/dL • No interference from unconjugated bilirubin up to 25 mg/dL • No interference from conjugated bilirubin up to 25 mg/dL • No interference from human IgG up to 5.3 g/dL • No interference from 55 commonly used pharmaceutical drugs. • Results should always be assessed in conjunction with the patient's medical history, clinical evaluation and other diagnostic procedures.	anticoagulant. Serum and blood or plasma specimens obtained using other anticoagulants (e.g. heparin or citrate) have not been evaluated and should not be used. • No interference from hemoglobin up to 10000 mg/dL • Severely hemolyzed specimens should be avoided • No interference from triglycerides up to 1000 mg/dL • No interference from cholesterol up to 1000 mg/dL • No interference from bilirubin up to 20 mg/dL • No interference from 55 commonly used pharmaceutical drugs. • Results should be evaluated in the context of all the clinical and laboratory data available.

(c) Analytical Comparison and Clinical Agreement

A paired comparison was performed at 2 clinical trial sites to assess the relationship of the ADVIA Centaur BNP assay to the predicate device. A total of 167 patients with heart failure (HF; clinical diagnoses of Class I – IV) and 20 individuals without heart failure (non-HF) were compared for both analytical and clinical agreement at a decision threshold of 100 pg/mL.

Analytical Comparison – ADVIA Centaur vs. Predicate Device

		Predicate Device		
		≥ 100 pg/mL	< 100 pg/mL	Total
Centaur	≥ 100 pg/mL	145	4	149
	< 100 pg/mL	6	32	38
	Total	151	36	187

	Estimate	95% Confidence Interval
% Analytical Agreement	94.7 % (177/187)	90.4% to 97.4%

Clinical Agreement – ADVIA Centaur BNP

		Clinical Status		
		HF	Non-HF	Total
Centaur	≥ 100 pg/mL	146	3	149
	< 100 pg/mL	21	17	38
	Total	167	20	187

	Estimate	95% Confidence Interval
% Clinical Agreement	87.2% (163/187)	81.5% to 91.6%
% Sensitivity	87.4% (146/167)	81.4% to 92.0%
% Specificity	85.0% (17/20)	62.1% to 96.8%

Clinical Agreement – Predicate Device

		Clinical Status		
		HF	Non-HF	Total
Predicate Device	≥ 100 pg/mL	146	5	151
	< 100 pg/mL	21	15	36
	Total	167	20	187

	Estimate	95% Confidence Interval
% Clinical Agreement	86.1% (161/187)	80.3% to 90.7%
% Sensitivity	87.4% (146/167)	81.4% to 92.0%
% Specificity	75.0% (15/20)	50.9% to 91.3%

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

JUN 23 2003

Kenneth T. Edds, Ph.D.
Manager, Regulatory Affairs
Bayer HealthCare LLC
Diagnostics Division
511 Benedict Avenue
Tarrytown, NY 10591-5097

Re: k031038
Trade/Device Name: Bayer Diagnostics ADVIA® Centaur® BNP Assay
Regulation Number: 21 CFR 862.1117
Regulation Name: B-type natriuretic peptide test systems
Regulatory Class: Class II
Product Code: NBC; JIT; JJX
Dated: March 31, 2003
Received: April 4, 2003

Dear Dr. Edds:

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 (301) 594-3084. 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 (301) 443-6597 or at its Internet address http://www.fda.gov/cdrh/dsma/dsmamain.html.

Sincerely yours,

Steven Gutman

Steven I. Gutman, M.D., M.B.A.
Director
Office of *In Vitro* Diagnostic Device
Evaluation and Safety
Center for Devices and
Radiological Health

Enclosure

510(k) Number (if known): K031038

Device Name: Bayer Diagnostics ADVIA® Centaur® BNP Assay

Indications for Use:

For *in vitro* diagnostic use in the quantitative determination of B-type Natriuretic Peptide (BNP) in human plasma using the ADVIA Centaur® System. This assay is indicated for the measurement of plasma BNP as an aid in the diagnosis of heart failure. This assay is not intended for use on any other system.

Division Sign-Off

Office of In Vitro Diagnostic Device Evaluation and Safety

510(k) K031038

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

Concurrence of CDRH, Office of Device Evaluation (ODE)

Prescription Use ✓ OR Over-The-Counter Use _____
(Per 21 CFR 801.109) (Optional Format 1-2-96)