FEB 15 2005

K043976

SUMMARY OF SAFETY AND EFFECTIVENESS INFORMATION

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:

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Date of Preparation:

December 14, 2004

Name of Product(s):

Stratus® CS Acute Care™ NT-proBNP (pBNP) TestPak assay
Stratus® CS pBNP CalPak (the assay calibrator)
Stratus® CS pBNP DilPak (the assay diluent)

FDA Classification Name(s):

B-type natriuretic peptide test system and calibrator (all Class II)

FDA Guidance Documents:

"Class II Special Control Guidance Document for B-Type Natriuretic Peptide Premarket Notifications; Final Guidance for Industry and FDA Reviewers" - 11/30/2000

Predicate Device(s):

Roche Diagnostics Elecsys® proBNP immunoassay and CalSet calibrator (K032646/K022516)

Device Description(s):

Method

The Stratus® CS Acute Care™ NT-proBNP method is a two-site sandwich assay based upon solid phase Radial Partition Immunoassay (RPIA) technology. In this procedure, dendrimer linked polyclonal antibody is added to the center portion of a square piece of glass fiber paper in the pBNP TestPak. This antibody recognizes a distinct antigenic site on the NT-proBNP molecule. Sample is then added onto the paper where it reacts with the immobilized antibody. After a short incubation, a conjugate consisting of enzyme-labeled polyclonal antibody directed against a second distinct antigenic site on the NT-proBNP molecule is pipetted onto the reaction zone of the paper. During this second incubation period, enzyme-labeled antibody reacts with the bound NT-proBNP , forming an antibody-antigen-labeled antibody sandwich. The unbound labeled antibody is later eluted from the field of view of the Stratus® CS analyzer by applying a substrate wash solution to the center of the reaction zone. By including substrate for the enzyme within the wash solution, initiation of enzyme activity occurs simultaneously with the wash. The enzymatic rate of the bound fraction increases directly with the concentration of NT-proBNP in the sample. The reaction rate can then be measured by an optical system that monitors the

reaction rate via front surface fluorescence. All data analysis functions are performed by the microprocessor within the analyzer.

Calibrator
The Dade Behring pBNP Calibrator is a frozen liquid product containing synthetic human NT-proBNP in a bovine albumin matrix with stabilizers and preservative. The kit consists of five CalPaks at a single calibrator level. Each CalPak contains calibrator reagent in three wells.

Diluent
The Dade Behring pBNP Diluent is a refrigerated product containing a buffered bovine protein matrix with stabilizers and preservative. The kit consists of 5 DilPaks with diluent in one well.

Intended Use:
Method
The Stratus® CS Acute Care™ NT-proBNP method (pBNP) is an *in vitro* diagnostic test for the quantitative measurement of N-terminal pro-brain natriuretic peptide (NT-proBNP) in heparanized plasma. In individuals suspected of having congestive heart failure (CHF), measurements of NT-proBNP are used as an aid in the diagnosis and assessment of severity. The test is further indicated for the risk stratification of patients with acute coronary syndrome and heart failure.

Calibrator
The NT-proBNP (pBNP) Calibrator (CalPak), REF CPBNP-C, is an *in vitro* diagnostic product intended to be used for calibration of the Stratus® CS Acute Care™ NT-proBNP method (pBNP).

Diluent
The NT-proBNP Dilution Pak (DilPak), REF CPBNP-D, is an *in vitro* diagnostic product intended to be used in conjunction with the pBNP TestPak, REF CPBNP, on the Stratus® CS analyzer for the measurement of samples with elevated levels of NT-proBNP.

Comparison to Predicate Device:
Method
A summary of the features of the Dade Behring Stratus® CS Acute Care™ pBNP TestPak and the predicate Roche Diagnostics Elecsys® proBNP immunoassay (K032646/K022516) is provided in the following charts. The Dade Behring pBNP TestPak utilizes the Roche polyclonal (sheep) antibody/antigen set.

Method:

Feature	Stratus® CS Acute Care™ pBNP	Roche Elecsys® proBNP
Intended Use	For the *in vitro* quantitative determination of N-terminal pro-brain natriuretic peptide in human plasma as an aid in the diagnosis and assessment of severity of individuals suspected of having congestive heart failure. The test is further indicated for the risk stratification of patients with acute coronary syndrome and heart failure.	For the *in vitro* quantitative determination of N-terminal pro-brain natriuretic peptide in human serum and plasma as an aid in the diagnosis of individuals suspected of having congestive heart failure. The test is further indicated for the risk stratification of patients with acute coronary syndrome and congestive heart failure.
Assay Type (detection)	immunoassay (fluorometric)	immunoassay (electrochemiluminescent)
Reportable Range	15- 20,000 pg/mL	5 - 35,000 pg/mL
Antibody	Roche Diagnostics' polyclonal (sheep) antibody	polyclonal (sheep) antibody
Cut-off	125 pg/mL for patients less than 75 years and 450 pg/mL for patients 75 years and older	125 pg/mL for patients less than 75 years and 450 pg/mL for patients 75 years and older
Analytical Sensitivity	15 pg/mL	5 pg/mL
Functional Sensitivity	< 50 pg/mL	< 50 pg/mL
Analytical Specificity	The pharmaceutical Natrecor® shows no significant cross reactivity at 0 and 125 pg/mL NT-proBNP; sixteen other substances also show no significant cross reactivity	The pharmaceutical Natrecor® shows no significant cross reactivity at 300 pg/mL and 3000 pg/mL NT-proBNP; sixteen other substances also show no significant cross reactivity

Interferences	No significant interference from: bilirubin, conj. up to 60 mg/dL bilirubin, unconjugated up to 60 mg/dL hemoglobin up to 1000 mg/dL triglycerides up to 3000 mg/dL rheumatoid factors up to 750 IU/mL	No significant interference from: bilirubin up to 35 mg/dL hemoglobin up to 1.4 g/dL triglycerides up to 4000 mg/dL rheumatoid factors up to 1500 IU/mL
Reference	Roche purified synthetic NT-proBNP (1-76)	Roche purified synthetic NT-proBNP (1-76)
Hook Effect	No high dose effect (up to 1,400,000 pg/mL)	No high dose effect (up to 300,000 pg/mL)
Calibration Interval	Calibration curve updated for each lot, using one level and every 30 days, thereafter with the same reagent lot. After calibration update at completion of each test, recovered values are calculated from stored calibration coefficients.	Calibration curve updated for each lot, using two levels every 30 days with the same reagent lot.
Sample Volume	50 uL	20 uL

Calibrator:

Feature	Stratus® CS Acute Care™ pBNP	Roche Elecsys® proBNP
Intended Use	pBNP method calibration	proBNP method calibration
Analyte	Synthetic NT-proBNP	Synthetic NT-proBNP
Matrix	Bovine albumin	Horse serum
Form	Liquid	Lyophilyzed
Volume	150 uL in each of three wells	1 mL for each level
Levels	1 level	2 levels (140 and 2700 pg/mL)

Method performance Summary:

Clinical Results

For the Reference Study Group, NT-proBNP concentrations were determined in 308 individuals without congestive heart failure (163 Women and 145 men); this population included apparently healthy individuals and individuals with diabetes, hypertension, and pulmonary disease. For the Disease Study Group, blood samples were obtained from 234 patients diagnosed with congestive heart failure (CHF); this population included 70 women and 164 men.

The high level of equivalence between the two assays on clinical performance measures justifies using the same cutoffs for the Stratus® CS Acute Care™ pBNP assay as the Elecsys® proBNP predicate device, as shown below:

Patients < 75 years: 125 pg/mL [14.8 pmol/L]
Patients ≥ 75 years: 450 pg/mL [53.2 pmol/L]

The clinical performance of the Dade Behring assay presented in the tables below was substantially equivalent to that of the predicate device. Data used to calculate the values are from the method comparison and reference interval data sets generated at the University of Maryland Medical Center.

Clinical Performance of Dade Behring NT-proBNP assay versus predicate device on Male patients.

Males		< 75 yrs (95% CI)	≥ 75 yrs (95% CI)
Sensitivity (%)	Stratus® CS pBNP	90% (84 – 95)	92% (84 – 99)
	Elecsys® proBNP	91% (86 – 96)	92% (84 – 99)
Specificity (%)	Stratus® CS pBNP	92% (86 – 98)	73% (61 – 84)
	Elecsys® proBNP	93% (87 – 98)	73% (61 – 84)
NPV	Stratus® CS pBNP	86% (79 – 94)	92% (84 – 100)
	Elecsys® proBNP	89% (82 – 95)	92% (84 – 100)

Clinical Performance of Dade Behring NT-proBNP assay versus predicate device on Female Patients

Females		< 75 yrs (95% CI)	≥ 75 yrs (95% CI)
Sensitivity (%)	Stratus® CS pBNP	84% (74 – 94)	95% (85 – 100)
	Elecsys® proBNP	84% (74 – 94)	95% (85 – 100)
Specificity (%)	Stratus® CS pBNP	92% (87 – 97)	85% (76 – 94)
	Elecsys® proBNP	94% (90 – 99)	87% (78 – 95)
NPV	Stratus® CS pBNP	92% (87 – 97)	98% (94 – 100)
	Elecsys® proBNP	92% (87 – 97)	98% (94 – 100)

Analytical Results

Method Comparison

A split sample method comparison demonstrated good agreement between the Dade Behring Stratus® CS Acute Care™ NT-proBNP TestPak method and the predicate Roche Elecsys® proBNP immunoassay with heparinized plasma patient samples.

Comparative Method	Slope	Intercept (pg/mL)	Correlation Coefficient	n
Roche Elecsys® proBNP	0.96	5.5	0.99	481

The model equation for Passing-Bablok linear regression statistics is: [results for Stratus® CS system] = slope x [comparative method results] + intercept. The range of NT-proBNP values in the correlation study was: 16.1 – 17691.9 pg/mL.

Lithium Heparin versus Sodium Heparin

Comparison of lithium heparin versus sodium heparin samples on the Stratus® CS system showed very good agreement. Lithium heparin samples (n=19) ranging from < 15 to 15,810 pg/mL when compared to sodium heparin samples gave a slope of 1.00, correlation coefficient of 0.999, and intercept of 28 pg/mL using Passing-Bablok regression statistics.

Reproducibility

Typical precision observed for the Stratus® CS NT-proBNP TestPak method is summarized below:

		Within-Run Precision		Total Precision	
Sample	**Mean (pg/mL)**	**SD (pg/mL)**	**%CV**	**SD (pg/mL)**	**%CV**
Human Plasma Pool					
Pool 1	153	6.5	4.2	7.8	5.1
Pool 2	463	15.0	3.2	15.0	3.2
Pool 3	6726	177.3	2.6	177.3	2.6
MAS® CardioImmune® proBNP Control					
Level 1	156	7.7	4.9	7.7	4.9
Level 2	5371	115.5	2.1	158.6	3.0

* MAS® and CardioImmune® are registered trademarks of Medical Analysis Systems, Inc., Camarillo, CA

The reproducibility testing was conducted in accordance with the NCCLS Approved Guideline for User Evaluation of Precision Performance of Clinical Chemistry Devices EP5-A, 1999. Specimens at each level were analyzed in duplicate once per day for 20 days. The within-run and total standard deviations were calculated by the analysis of variance method.

Calibrator

The Stratus® CS pBNP CalPak is similar to other calibrator products associated with their assays, such as the Roche Elecsys® proBNP CalSet calibrator.

Diluent

The Stratus® CS pBNP DilPak is similar to other diluent products associated with their assays, such as the Roche Elecys® proBNP CalSet diluent.

Comments on Substantial Equivalence:
Both the Stratus® CS Acute Care™ NT-proBNP (pBNP) TestPak and the Roche Elecsys® proBNP immunoassays are intended for the quantitative determination of NT-proBNP. Comparative data for human plasma samples demonstrate good analytical and clinical agreement between the methods.

Conclusion:
The Dade Behring ® CS Acute Care™ NT-proBNP (pBNP) TestPak and the predicate Roche Elecsys® proBNP immunoassay (K032646/K022516) are substantially equivalent based on their intended use and performance characteristics as described above. The calibrator and diluent products are also equivalent in their design and intended use with their respective assay systems.

George M. Plummer
Regulatory Affairs and Compliance Manager
December 14, 2004

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

FEB 15 2005

Mr. George M. Plummer
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Re: k043476
Trade/Device Name: Stratus® CS Acute Care™ NT-proBNP (pBNP) TestPak assay
Stratus® CS pBNP CalPak
Stratus® CS pBNP DilPak
Regulation Number: 21 CFR 862.1117
Regulation Name: B-type natriuretic peptide test system
Regulatory Class: Class II
Product Code: NBC; JIT
Dated: December 14, 2004
Received: December 16, 2004

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)276-0484. 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/industry/support/index.html

Sincerely yours,

Jean M. Cooper MS, DVM

Jean M. Cooper, MS, 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): K043476

Device(s) Name(s):

Stratus® CS Acute Care™ NT-proBNP (pBNP) TestPak assay
Stratus® CS pBNP CalPak
Stratus® CS pBNP DilPak

Indications for Use:

The Stratus® CS Acute Care™ NT-proBNP method (pBNP) is an *in vitro* diagnostic assay for the quantitative determination of N-terminal pro-brain natriuretic peptide (NT-proBNP) in human plasma. In individuals suspected of having congestive heart failure (CHF), measurements of NT-proBNP are used as an aid in the diagnosis and assessment of severity. The test is further indicated for the risk stratification of patients with acute coronary syndrome and heart failure.

The NT-proBNP Calibrator (pBNP CalPak) is an *in vitro* diagnostic product intended to be used for calibration of the NT-proBNP method on the Stratus® CS analyzer.

The NT-proBNP Dilution Pak (DilPak) is an *in vitro* diagnostic product intended to be used for dilution of the NT-proBNP Method on the Stratus® CS analyzer.

✓

Prescription Use _____ **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)

(Division Sign-Off)
Division of Clinical Laboratory Devices
510(k) Number K043476