

**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY TEMPLATE**

A. 510(k) Number:

k060548

B. Purpose for Submission:

Submission for new indications for Point of Care (POC) use

C. Measurand:

Human chorionic gonadotropin and NT-ProBNP

D. Type of Test:

Quantitative immunoassay

E. Applicant:

Dade Behring, Inc.

F. Proprietary and Established Names:

Stratus CS Acute Care Beta hCG TestPak and NT-PROBNP and TestPak Assay,
CalPak and DilPak

G. Regulatory Information:

1. Regulation section:

21CFR Sec.- 862.1155-Human chorionic gonadotropin (HCG) test system.

21CFR Sec.-862.1117-B-type natriuretic peptide test system.

21CFR Sec.- 862.1150 Calibrator.

2. Classification:

Class 2

3. Product code:

DHA - System, test, human chorionic gonadotropin

NBC - Test, natriuretic peptide

JIT - Calibrator, secondary

4. Panel:

Chemistry (75)

H. Intended Use:

1. Intended use(s):

See Indications for use below.

2. Indication(s) for use:

The Stratus CS Acute Care™ β hCG method is an *in vitro* diagnostic test for the

quantitative measurement of the total beta subunit, vis, both the intact hCG dimer and the free β subunit, of the human chorionic gonadotropin hormone in heparinized plasma. β hCG is used for the early detection of pregnancy. This method is for use by trained health care professionals in the clinical laboratory and point of care (POC) settings.

The Stratus CS Acute Care™ β hCG Calibrator (β hCG CalPak) is an *in vitro* diagnostic product intended to be used for calibration of the Stratus® CS Acute Care™ β hCG method.

The Stratus CS Acute Care™ β hCG Dilution Pak (β hCG DilPak) is an *in vitro* diagnostic product intended to be used in conjunction with the Acute Care™ β hCG TestPak for the measurement of samples with elevated levels of β hCG.

The Stratus CS Acute Care™ NT-proBNP method is an *in vitro* diagnostic test for the quantitative measurement of N-terminal pro-brain natriuretic peptide (NT-proBNP) in heparinized 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. This method is for use by trained health care professionals in the clinical laboratory and point of care (POC) settings.

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

The Stratus CS Acute Care™ NT-proBNP Dilution Pak (pBNP DilPak) is an *in vitro* diagnostic product intended to be used in conjunction with the Acute Care™ pBNP TestPak for the measurement of samples with elevated levels of NT-proBNP.

3. Special conditions for use statement(s):
For prescription use
4. Special instrument requirements:
Stratus® CS Analyzer

I. Device Description:

β hCG Method

The Stratus® CS Acute Care™ β hCG method is a solid phase, two-site sandwich fluorometric immunoassay based upon Radial Partition Immunoassay (RPIA) technology. In this procedure, dendrimer linked monoclonal β hCG antibody is added to the center portion of a square piece of glass fiber paper in the β hCG TestPak. The dendrimer binds electrostatically to the glass fibers and immobilizes the capture antibody to the paper. Sample is then added, whereupon β hCG reacts with the

immobilized antibody. After a short incubation, a conjugate, consisting of enzyme-labeled (alkaline phosphatase) monoclonal antibody directed against a distinct antigenic site on the β hCG molecule, is pipetted onto the reaction zone of the paper. During this second incubation period, the unbound, labeled antibody is radially eluted with a wash solution. By including substrate (4-methylumbelliferyl phosphate) 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 β hCG in the sample. Utilization of two monoclonal antibodies which are specific for distinct antigenic sites on the β subunit of hCG allows the assay to measure the total β hCG in the sample, viz, both the intact hCG dimer and the free β subunit. Concentration is 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 Stratus® CS Acute Care β hCG calibrator (β hCG CalPak) contains human hCG in a bovine serum matrix with preservatives. The β hCG CalPak is a single-use liquid product which contains one calibrator level at an approximate concentration of 950 mIU/mL* [IU/L] in each of three wells. The kit consists of five CalPaks at a single calibrator level.

Diluent

The Stratus® CS Acute Care β hCG Diluent (β hCG DilPak) contains a liquid buffered bovine protein matrix with stabilizers and 0.09% sodium azide. The kit consists of 5 DilPaks with diluent in one well.

NT-proBNP 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 Stratus® CS Acute Care 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 Stratus® CS Acute Care 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

J. Substantial Equivalence Information:

1. Predicate device name(s):

Dade Behring Stratus® CS β hCG TestPak, CalPak and DilPak

Dade Behring Stratus® CS pBNP Acute Care™ TestPak, CalPak and DilPak

2. Predicate 510(k) number(s):

k003696, k043476 respectively

3. Comparison with predicate:

The modification of these two methods is the addition of point of care use to the intended use. There are no formulation or design changes associated with the intended use change. The two products are identical and use the same manufacturing processes. Labeling changes reflect the new intended use and supporting data in addition to minor format changes.

K. Standard/Guidance Document Referenced (if applicable):

- "Bundling Multiple Devices or Multiple Indications in a Single Submission"- Guidance for Industry and FDA Staff - 11/26/2003
- Class II Special Control Guidance Document for B-Type Natriuretic Peptide Premarket Notifications; Final Guidance for Industry and FDA Reviewers" - 11/30/2000

L. Test Principle:

See Device Description in Section I. above

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

A precision study was conducted using plasma pools (PP) at two concentrations for β hCG and three concentrations for PBNP on the Stratus® CS analyzer. The materials were processed in replicates of four (the instrument can process only up to four Paks at any one time) over a period of five days by Lab, ED and CCU personnel on the instruments located in their respective areas. The data was calculated according to the NCCLS EP15-A

(December 2001). The results are summarized in the tables below:

βhCG in mIU/mL							
Location	Plasma Pools	N	Mean	Within run		Total	
				SD	%CV	SD	%CV
Lab	PP 1	20	23.7	0.66	2.8	1.06	4.5
ED	PP 1	20	24.0	0.69	2.9	0.69	2.9
CCU	PP 1	20	23.9	0.72	3.0	0.72	3.0
Lab	PP 2	20	583.7	20.08	3.4	24.66	4.2
ED	PP 2	20	591.7	15.91	2.7	15.91	2.7
CCU	PP 2	20	579.2	16.30	2.9	18.46	3.2

PBNP in pg/mL - Site 1							
Location	Plasma Pools	N	Mean	Within run		Total	
				SD	%CV	SD	%CV
Lab	PP 1	20	120.9	4.97	4.1	4.97	4.1
ED	PP 1	20	126.7	6.98	5.5	7.26	5.7
CCU	PP 1	20	116.6	6.50	5.6	6.71	5.8
Lab	PP 2	20	366.9	11.12	3.0	17.03	4.6
ED	PP 2	20	374.6	10.58	2.8	11.35	3.0
CCU	PP 2	20	359.0	12.82	3.6	15.43	4.3
Lab	PP 3	20	5669.7	124.30	2.2	124.3	2.2
ED	PP 3	20	5745.7	67.05	1.2	67.05	1.2
CCU	PP 3	20	5623.8	136.93	2.4	152.91	2.7

PBNP in pg/mL - Site 2							
Location	Plasma Pools	N	Mean ^o	Within run		Total	
				SD	%CV	SD	%CV
Lab	PP 1	20	125.0	6.05	4.8	6.6	5.3
ED	PP 1	20	118.1	6.52	5.5	6.73	5.7
CCU	PP 1	20	148.5	7.48	5.0	8.42	5.7
Lab	PP 2	20	377.5	8.84	2.3	9.0	2.4
ED	PP 2	20	371.8	7.24	1.9	9.35	2.5
CCU	PP 2	20	404.7	4.84	1.2	5.66	1.4
Lab	PP 3	20	5891.9	154.42	2.6	185.56	3.1
ED	PP 3	20	5971.4	92.83	1.6	112.63	1.9
CCU	PP 3	20	5893.1	151.09	2.6	156.57	2.7

^o CCU performed testing with a different lot of TestPaks

- b. *Linearity/assay reportable range:*
See k003696 and k043476
 - c. *Traceability, Stability, Expected values (controls, calibrators, or methods):*
See k003696 and k043476
 - d. *Detection limit:*
See k003696 and k043476
 - e. *Analytical specificity:*
See k003696 and k043476
 - f. *Assay cut-off:*
See k003696 and k043476
2. Comparison studies:
- a. *Method comparison with predicate device:*

To demonstrate that data generated by “non-laboratory” personnel is comparable to precision and data generated by “laboratory” personnel, method comparison and precision analysis were performed at three different locations: the clinical laboratory (LAB), Emergency Department (ED) and Cardiac Care Unit (CCU) at one external evaluation site for β hCG and two external evaluation sites for NT-proBNP, using personnel representative of POC users.

β hCG

Method comparison studies were conducted at multiple sites in one institution comparing the performance obtained with the Stratus® CS Acute Care™ β hCG and NT proBNP (pBNP) TestPaks with non-laboratory personnel versus laboratory personnel. Data from non-laboratory personnel was obtained in the Emergency Department (ED) and the Critical Care Unit (CCU) at the evaluation sites. The results are summarized in the tables below:

β hCG				
Locations	N	Slope	Intercept	R
Lab v ED	67	1.02	-0.5	0.999
Lab v CCU	66	0.97	3.1	0.999

PBNP – Site 1				
Locations	N	Slope	Intercept	R
Lab v ED	66	1.00	25.9	0.998
Lab v CCU	63	0.98	9.2	0.998

PBNP – Site 2				
Locations	N	Slope	Intercept	R
Lab v ED	60	1.01	-19.8	0.999
Lab v CCU	60	1.03	-17.3	0.999

- b. *Matrix comparison:*
Not applicable
- 3. Clinical studies:
 - a. *Clinical Sensitivity:*
See k003696 and k043476
 - b. *Clinical specificity:*
See k003696 and k043476
 - c. Other clinical supportive data (when a. and b. are not applicable):
See k003696 and k043476
- 4. Clinical cut-off:
See k003696 and k043476
- 5. Expected values/Reference range:
See k003696 and k043476

N. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

O. Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.