

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

**A. 510(k) Number:**

K032646

**B. Analyte:**

B-type natriuretic peptide test system (BNP)

**C. Type of Test:**

Quantitative

**D. Applicant:**

Roche Diagnostics

**E. Proprietary and Established Names:**

Elecsys® proBNP assay

**F. Regulatory Information:**

1. Regulation section:  
862.1117 B-type natriuretic peptide test system
2. Classification:  
Class II
3. Product Code:  
NBC
4. Panel:  
75

**G. Intended Use:**

1. Indication(s) for use:  
For the *in vitro* quantitative determination of N-terminal proBrain natriuretic peptide in human serum and plasma. Elecsys proBNP is used 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. The electrochemiluminescence immunoassay "ECLIA" is intended for use on the Roche Elecsys 1010, Elecsys 2010, and Modular Analytics E170.
2. Special condition for use statement(s):
3. Special instrument Requirements:

**H. Device Description:**

The Elecsys® proBNP reagent kit is supplied as a 100 test kit. The kit contains the following:

- M Streptavidin-coated microparticles, 1 bottle, 6.5 ml: streptavidin-coated microparticles, 0.72mg/ml; binding capacity: 470 ng biotin/mg microparticles; preservative
- R1 Anti-NT proBNP-AB-biotin, 1 bottle, 9ml: Biotinylated polyclonal anti-NT-proBNP antibody (sheep) 1.5 µg/ml; phosphate buffer 40 mmol/l, pH 7.4; preservative
- R2 Anti-NT-proBNP-Ab-Ru(bpy), 1 bottle, 9ml: polyclonal anti-NT-proBNP antibody (sheep) labeled with ruthenium complex 1.7 µg/ml; phosphate buffer 40 mmol/l, pH 7.4; preservative

**I. Substantial Equivalence Information:**

1. Predicate device name(s):  
Roche Diagnostics Elecsys® proBNP assay
2. Predicate K number(s):  
K022516
3. Comparison with predicate:

<b>Similarities</b>		
<b>Item</b>	<b>K032646</b>	<b>K022516</b>
Test principle	Same as K022516	Electrochemiluminescent assay
Sample type	Same as K022516	Serum and plasma
Measuring range	Same as K022516	5-35,000 pg/ml
Instrument	Same as K022516	Roche Elecsys 1010, Elecsys 2010, and Modular Analytics E170
Cut-off	Same as K022516	125 pg/ml for patients younger than 75 years and 450 pg/ml for patients 75 years and older
<b>Differences</b>		
<b>Item</b>	<b>K032646</b>	<b>K022516</b>
Indications for Use	For the <i>in vitro</i> quantitative determination of N-terminal proBrain natriuretic peptide in human serum and plasma. Elecsys proBNP is used as an aid in the diagnosis of individuals suspected of having congestive heart failure.	For the <i>in vitro</i> quantitative determination of N-terminal proBrain natriuretic peptide in human serum and plasma. Elecsys proBNP is used 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.	
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**J. Standard/Guidance Document Referenced (if applicable):**

NCCLS EP-5A, Class II Special Control Guidance Document for B-Type Natriuretic Peptide Pre-Market Notifications; Final Guidance for Industry and FDA Reviewers

**K. Test Principle:**

The Elecsys® proBNP Test System is an electrochemiluminescence immunoassay (ECLIA). The test uses the sandwich principle. In the first incubation, antibody from the sample, biotinylated polyclonal NT-proBNP-specific antibody and polyclonal NT-proBNP-specific antibody labeled with a ruthenium complex form a sandwich complex. In the second incubation, after addition of streptavidin labeled microparticles, the complex produced is bound to the solid phase via biotin-streptavidin interaction. The reaction mixture is aspirated into the measuring cell where the microparticles are magnetically captured onto the surface of the electrode. Application of a voltage to the electrode then induces chemiluminescent emission which is measured by a photomultiplier. Results are determined via a calibration curve. This curve is instrument-specifically generated by a 2-point calibration and a master curve provided via the reagent barcode.

**L. Performance Characteristics (if/when applicable):**

1. Analytical performance:

a. *Precision/Reproducibility:*

Previously established for K022516. Reproducibility was determined using Elecsys reagents, pooled human sera and controls in a modified protocol (NCCLS EP-5A). Samples were run 6 times daily for 10 days (n =60) for the 1010 and 2010. For the E170, n = 21. Within run precision (% CV) ranged from 0.9 to 3.0 %, with total precision from 2.2 to 5.8 %.

b. *Linearity/assay reportable range:*

Previously established for K022516. Assay is linear up to 35,000 pg/ml.

c. *Traceability (controls, calibrators, or method):*

Reference standard is purified synthetic NTG-proBNP (1-76) in human serum matrix.

d. *Detection limit:*

Previously established for K022516. Analytical sensitivity (lower detection limit) is 5 pg/ml. Functional sensitivity (the lowest NT-

proBNP concentration that can be reproducibly measured with a between-run coefficient of variation of 20 %) is < 50 pg/ml.

*e. Analytical specificity:*

Previously established for K022516. No significant interference was seen from bilirubin up to 35 mg/dL, hemoglobin up to 1.4 g/dL, triglyceride up to 4000 mg/dl, biotin < 30 ng/ml, and rheumatoid factor up to 1500 IU/ml. In vitro tests were performed on 51 commonly used pharmaceuticals. No interference was found. The pharmaceutical Natrecor® does not show cross reactivity with the Elecsys proBNP assay.

*f. Assay cut-off:*

Previously established for K022516. 125 pg/ml for patients younger than 75 years and 450 pg/ml for patients 75 years and older.

2. Comparison studies:

*a. Method comparison with predicate device:*

The only difference between K032646 and the predicate K022516 is the change in the Indications for Use. K032646 and K022516 are identical assays, therefore, no method comparison was performed.

*b. Matrix comparison:*

Previously established for K022516. Serum and heparinized plasma are the recommended sample types for this assay. The criteria used for acceptability was recovery between 90 - 110 % of the serum value or slope 0.9 - 1.1 + coefficient of correlation > 0.95 + intercept within  $\pm 2$  analytical sensitivity. When EDTA plasma is used, the values found are approximately 10 % lower.

3. Clinical studies:

*a. Clinical sensitivity:*

Previously established for K022516.

### Sensitivity and Specificity vs. Age and Gender

Males	< 45 years	45-54 years	55-64 years	65-74 years	75 + years	< 75 years
% Sensitivity	81.6	88.2	89.6	91.7	86.5	89.0
95% confidence interval	68.0-91.24	81.27-93.24	84.47-93.42	85.58-95.77	74.21-94.47	85.95-91.58
% specificity	95.7	93.3	87.8	86.7	88.9	90.0
95% confidence interval	78.05-99.89	89.07-96.31	82.33-91.99	75.59-92.07	77.37-95.81	87.14-92.32
Prevalence	0.7	1.8	6.2	6.8	9.8	1.39
Negative predictive value	100.0	99.8	99.2	99.3	96.8	99.8

Females	< 45 years	45-54 years	55-64 years	65-74 years	75 + years	< 75 years
% Sensitivity	86.7	90.5	89.3	94.3	81.8	90.6
95% confidence interval	59.54-98.34	69.62-98.83	78.12-95.97	80.84-99.30	64.54-93.02	84.08-95.02
% specificity	84.9	85.5	79.9	57.8	87.9	76.7
95% confidence interval	68.1-94.89	80.64-89.53	74.52-84.63	50.21-65.09	77.51-94.62	73.47-79.72
Prevalence	0.5	1.3	3.4	6.6	9.7	1.16
Negative predictive value	100.0	99.9	99.5	99.3	97.8	99.9

- b. *Clinical specificity:*  
see clinical sensitivity
- c. *Other clinical supportive data (when a and b are not applicable):*  
Three peer reviewed literature references are provided demonstrating clinical support of the additional indications for use for the risk stratification of patients with acute coronary syndrome and congestive heart failure. All three studies measured NT-proBNP using the Elecsys proBNP immunoassay. The studies are:

Reference 1: N-Terminal Pro-Brain Natriuretic Peptide and Other Risk Markers for the Separate Prediction of Mortality and Subsequent Myocardial Infarction in Patients with Unstable Coronary Artery Disease, GUSTO IV Substudy, James, S.K. et al, Circulation 2003;108: 275-281.

Reference 2: N-Terminal Pro-Brain Natriuretic Peptide on Admission for Early Risk Stratification of Patients with Chest Pain and No ST-Segment Elevation, Jernberg, T. et al. Journal of the American College of Cardiology Vol 40, No. 3, 2002: 437-445.

Reference 3: N-Terminal pro B type natriuretic peptide, but not the new putative cardiac hormone relaxin, predicts prognosis in patients with chronic heart failure. Fisher, C. et al. Heart 2003; 89:879-881.

- 4. Clinical cut-off:  
Previously established for K022516. 125 pg/ml for patients younger than 75 years and 450 pg/ml for patients 75 years and older.
- 5. Expected values/Reference range:  
see clinical cut-off

#### **M. Conclusion:**

Based upon a review of the information presented in this PMN, I recommend that this device is substantially equivalent to devices regulated by 21 CFR 862.1117, 75 NBC, B-type natriuretic peptide test system, Class II.