

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

A. 510(k) Number:

K051382

B. Purpose for Submission:

Expansion of indication for use

C. Measurand:

N-terminal proBrain natriuretic peptide (proBNP)

D. Type of Test:

Quantitative immunoassay

E. Applicant:

Roche Diagnostics

F. Proprietary and Established Names:

Elecsys proBNP Immunoassay

G. Regulatory Information:

1. Regulation section:

21 CFR §862.1117; B-type natriuretic peptide test system

2. Classification:

Class II

3. Product code:

NBC

4. Panel:

Chemistry (75)

H. Intended Use:

1. Intended use(s):

See indications for use below.

2. 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 or congestive heart failure. The test may also serve as an aid in the assessment of increased risk of cardiovascular events and mortality in patients at risk for heart failure who have stable coronary artery disease.

The electrochemiluminescence immunoassay "ECLIA" is intended for use on the Roche Elecsys 1010, Elecsys 2010 and MODULAR ANALYTICS E170 immunoassay analyzers.”

3. Special conditions for use statement(s):

None noted.

4. Special instrument requirements:
See the Indications for Use above.

I. Device Description:

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

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

J. Substantial Equivalence Information:

1. Predicate device name(s):
Roche Diagnostics Elecsys® proBNP Immunoassay
2. Predicate 510(k) number(s):
k022516 – original submission
k032646 – expansion to include stratification of patients with acute coronary syndrome and congestive heart failure.
3. Comparison with predicate:

Similarities		
Item	K051382	K032646
Test principle	Same as K032646	Electrochemiluminescent assay
Sample type	Same as K032646	Serum and plasma
Measuring range	Same as K032646	5-35,000 pg/ml
Instrument	Same as K032646	Roche Elecsys 1010, Elecsys 2010, and Modular Analytics E170
Cut-off	Same as K032646	125 pg/ml for patients younger than 75 years and 450 pg/ml for patients 75 years and older

Differences		
Item	K051382	K032646

Indications for Use	<p>For the <i>in vitro</i> quantitative determination of N-terminal proBrain natriuretic peptide in human serum and plasma.</p> <p>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 or congestive heart failure. The test may also serve as an aid in the assessment of increased risk of cardiovascular events and mortality in patients at risk for heart failure who have stable coronary artery disease.</p>	<p>For the <i>in vitro</i> quantitative determination of N-terminal proBrain natriuretic peptide in human serum and plasma.</p> <p>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.</p>
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K. Standard/Guidance Document Referenced (if applicable):

None referenced in this submission.

L. Test Principle:

The Elecsys® proBNP Immunoassay 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.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:
 - a. *Precision/Reproducibility:*
Established in k022516 and k032646.
 - b. *Linearity/assay reportable range:*
Established in k022516 and k032646.
 - c. *Traceability, Stability, Expected values (controls, calibrators, or methods):*
Established in k022516 and k032646.
 - d. *Detection limit:*
Established in k022516 and k032646.
 - e. *Analytical specificity:*
Established in k022516 and k032646.
 - f. *Assay cut-off:*
Established in k022516 and k032646; 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 K051382 and the predicate K032646 is the change in the Indications for Use. K051382 and K032646 are identical assays; therefore, no method comparison was performed.
 - b. *Matrix comparison:*
Previously established for K022516.
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 specificity above.

c. *Other clinical supportive data (when a. and b. are not applicable):*

Three peer reviewed literature references were provided, demonstrating clinical support of the additional indications for use as an aid in the assessment of increased risk of cardiovascular events and mortality in patients at risk for heart failure who have stable coronary artery disease. All three studies measured NT-proBNP using the Elecsys proBNP Immunoassay. The studies are:

Schnabel R, Rupprecht HJ, Lackner KJ, Lubos E, Bickel C, et al. Analysis of N-Terminal-pro-Brain Natriuretic Peptide and C-Reactive Protein for Risk Stratification in Stable and Unstable Coronary Artery Disease: Results from the AtheroGene Study. *European Heart Journal*, 2005. 26(3):241-249.

Kragelund C, Groenning B, Kober L, Hildebrandt P and Steffensen R. N-Terminal Pro-B-Type Natriuretic Peptide and Long-Term Mortality in Stable Coronary Heart Disease. *The New England Journal of Medicine*, 2005. 352(7):666-675.

Ndrepepa G, Braun S, Niemoller K, Mehilli J, von Beckerath N, et al. Prognostic Value of N-Terminal Pro-Brain Natriuretic Peptide in Patients with Chronic Stable Angina. *Circulation*, 2005. 112:2102-2107.

4. Clinical cut-off:

Previously established in 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 above.

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.