

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

A. 510(k) Number:

k051297

B. Purpose for Submission:

New Device

C. Measurand:

Osteocalcin
Calibrator
Calibration Verification Material

D. Type of Test:

Quantitative

E. Applicant:

Roche Diagnostics

F. Proprietary and Established Names:

Elecsys N-MID Osteocalcin Immunoassay
Elecsys N-MID Osteocalcin CalSet
Elecsys N-MID Osteocalcin CalCheck

G. Regulatory Information:

1. Regulation section:

21 CFR 862.1050 – Alkaline phosphatase or isoenzymes test system
21 CFR 862.1150 – Calibrator
21 CFR 862.1660 – Quality control material (assayed and unassayed)

2. Classification:

Class II – assay
Class II - calibrator
Class I reserved – calibrator verification material

3. Product code:

NEO - system, test, osteocalcin

JIT – calibrator, secondary

JJX – single (specified) analyte controls (assayed and unassayed)

4. Panel:

Chemistry (75)

H. Intended Use:

1. Intended use(s):

Elecsys N-MID® Osteocalcin: Immunoassay for the in vitro quantitative determination of N-MID® osteocalcin in human serum and plasma. The determination of osteocalcin, an indication of human bone formation and osteoblastic activity, may be useful as an aid in the management of postmenopausal osteoporosis. The electrochemiluminescence immunoassay “ECLIA” is intended for use on the Roche Elecsys 1010/2010 and MODULAR ANALYTICS E170 (Elecsys module) immunoassay analyzers.

Elecsys N-MID® Osteocalcin CalSet is used for calibrating the quantitative Elecsys N-MID Osteocalcin assay on the Elecsys immunoassay systems.

Elecsys N-MID® Osteocalcin CalCheck: For use in the verification of the calibration established by the Elecsys Osteocalcin reagent on Elecsys 1010/2010/MODULAR ANALYTICS E170 immunoassay analyzers.

2. Indication(s) for use:

Elecsys N-MID® Osteocalcin: Immunoassay for the in vitro quantitative determination of N-MID osteocalcin in human serum and plasma. The determination of osteocalcin, an indication of human bone formation and osteoblastic activity, may be useful as an aid in the management of postmenopausal osteoporosis.

The electrochemiluminescence immunoassay “ECLIA” is intended for use on the Roche Elecsys 1010/2010 and MODULAR ANALYTICS E170 (Elecsys module) immunoassay analyzers.

For prescription use only.

Elecsys N-MID® Osteocalcin CalSet is used for calibrating the quantitative Elecsys N-MID Osteocalcin assay.

The electrochemiluminescence immunoassay “ECLIA” is intended for use on the Roche Elecsys 1010/2010 and MODULAR ANALYTICS E170 (Elecsys module) immunoassay analyzers.

For prescription use only.

Elecsys N-MID® Osteocalcin CalCheck: For use in the verification of the calibration established by the Elecsys Osteocalcin reagent.

The electrochemiluminescence immunoassay “ECLIA” is intended for use on the Roche Elecsys 1010/2010 and MODULAR ANALYTICS E170 (Elecsys module) immunoassay analyzers.

For prescription use only.

3. Special conditions for use statement(s):

These devices are for prescription use.

4. Special instrument requirements:

Roche Elecsys 1010/2010 and MODULAR ANALYTICS E170 (Elecsys module) immunoassay analyzers.

I. Device Description:

The Elecsys N-MID Osteocalcin Assay reagent kit consists of 1 6.5 mL bottle of streptavidin-coated microparticles, 1 10 mL bottle of R1, and 1 10 mL bottle of R2. R1 contains biotinylated monoclonal anti-N-MID Osteocalcin antibody (mouse). R2 contains monoclonal anti-N-MID Osteocalcin antibody (mouse) labeled with ruthenium complex. The kit contains reagents sufficient for 100 tests.

The Elecsys N-MID Osteocalcin CalSet consists of 2 bottles, each for 1.0 mL of calibrator 1 and 2 bottles, each for 1.0 mL of calibrator 2. The calibrators contain synthetic peptide (at approximately 0 ng/mL and approximately 280 ng/mL) in a human serum matrix. The CalSet reagents are supplied lyophilized.

The Elecsys Osteocalcin CalCheck consists of 3 1.0 mL bottles of osteocalcin in analyte-free human serum. The target CalCheck values are approximately 30 ng/mL, 100 ng/mL, and 250 ng/mL. are lyophilized products consisting of human serum with added osteocalcin. The CalCheck reagents are supplied lyophilized.

J. Substantial Equivalence Information:

1. Predicate device name(s):

N-MID Osteocalcin One Step Elisa assay
 Elecsys C-Peptide CalSet
 Elecsys C-Peptide CalCheck

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

k003609
 k033873
 k040157

3. Comparison with predicate:

Similarities		
Item	Device	Predicates
Intended Use	Quantitative determination of osteocalcin	Same
Specimen	Human serum and plasma	Same
Sensitivity	0.5 ng/mL	Same
CalSet Levels	Two	Same
CalCheck Levels	Three	Same
Format – CalSet/CalCheck	Lyophilized	Same

Differences		
Item	Device	Predicate
Indications for Use	To aid in the management of postmenopausal osteoporosis	To aid in the prevention of osteoporosis
Assay Principle	Electrochemiluminescent immunoassay	Enzyme immunological test
Instrumentation	Roche Elecsys 1010/2010 and MODULAR ANALYTICS E170	Microtiter plate reader
Intended Use – Calibrator	For calibrating the quantitative Elecsys Osteocalcin assay	For calibrating the quantitative Elecsys C-Peptide assay

Differences		
Item	Device	Predicate
Intended Use – Calibration Verification Material	For use in the verification of the calibration established by the Elecsys Osteocalcin	For verification of the calibration established by the Elecsys C-Peptide reagent

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

CLSI Document EP5-A, Evaluation of Precision Performance of Clinical Chemistry Devices

L. Test Principle:

The Elecsys N-MID Osteocalcin Assay is a two step sandwich immunoassay with streptavidin microparticles and electrochemiluminescence detection. Results are determined using a calibration curve that is generated specifically on each instrument by a 2 point calibration and a master curve provided with the reagent bar code.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

Precision was determined using Elecsys reagents on the Elecsys® 2010 Immunoassay Analyzer, pooled human sera, and controls in a modified CLSI replication experiment. Six replicates of each control or sample (pooled human sera) were tested per day for 10 days. Within-run and total precision were calculated according to EP5-A.

The mean values for the three sera were 15.5 ng/mL, 13.7 ng/mL, and 68.3 ng/mL. The mean values for the three controls were 21.9 ng/mL, 105.7 ng/mL, and 205.5 ng/mL. The within-run precision yielded CVs ranging from 1.2% to 4.0%. The total precision yielded CVs ranging from 1.7% to 6.5%.

Precision was also determined using the Elecsys E170 analyzer. The mean values for the sera were 6.95 ng/mL, 24.8 ng/mL, and 76.4 ng/mL. The mean values for the controls were 22.2 ng/mL, 94.9 ng/mL, and 196 ng/mL. The within-run precision (n=21) yielded CVs ranging from 0.5% to 1.1%. The total precision yielded CVs ranging from 1.1% to 1.6%.

Precision data on Elecsys 1010 are maintained on file at Roche.

b. Linearity/assay reportable range:

The linearity of the Elecsys® N-MID Osteocalcin Assay was evaluated on the Elecsys® 2010 Immunoassay Analyzer by diluting three patient samples with varying amounts of the Elecsys® Universal Diluent.

The expected values were generated using the concentrations measured in the diluent and the undiluted sample and then applying the dilution factors. The percent recovery was determined by dividing the measured concentration with the expected concentration. Three serum samples (34.1 ng/mL, 135 ng/mL, and 211.7 ng/mL) yielded recoveries ranging from 91.3% to 102.1%.

Two additional dilution studies were performed to support linearity between 212 and 300 ng/mL, the upper limit of the measuring range. The 265.6 ng/mL and 277.4 ng/mL samples yielded recoveries ranging from 91.8% to 105.3%.

To assess hook effect, a sample was spiked with osteocalcin to a concentration of 4200 ng/mL diluted using Elecsys® Universal Diluent, and tested. No high-dose hook effect was observed.

c. Traceability, Stability, Expected values (controls, calibrators, or methods):

The Elecsys Osteocalcin assay has been standardized against in-house reference standards: osteocalcin in analyte-free human serum matrix.

The CalSet and CalCheck were prepared exclusively from the blood of donors tested individually and shown by FDA-approved methods to be free from HBsAg and antibodies to HCV and HIV.

Values are assigned using four Elecsys® MODULAR ANALYTICS E170 Immunoassay Analyzers, four Elecsys® 2010 Immunoassay Analyzers, and four Elecsys® 1010 Immunoassay Analyzers. Two independent series of analyses are performed on each instrument. Two-fold determinations are made for each sample. The target value is then calculated as the median of the determined values.

Accelerated stability data (35°C for 3 weeks) and reconstituted stability data were provided to support insert claims for Osteocalcin CalSet. The acceptance criterion for each study was based on signal recovery of 95-105% of the reference value.

Accelerated stability data (35°C for 3 weeks) and reconstituted stability data were also provided to support insert claims for Osteocalcin CalCheck. The acceptance criterion for each study was recovery of 90-110% of the reference value.

d. Detection limit:

The lower detection limit of the Elecsys® N-MID Osteocalcin Assay (0.500 ng/mL) was determined on the Elecsys® 2010 Immunoassay Analyzer by calculating the concentration of osteocalcin that would give a response equal to the mean of the Osteocalcin Master Low calibrator plus two standard deviations. Three runs of twenty-one replicates each of the low calibrator were performed. The calculated mean LDL for the three runs was 0.21 ng/mL.

e. Analytical specificity:

To evaluate potential assay interference from endogenous substances, three samples spiked with different amounts of an interferent (one interferent per sample) were evaluated. Also, each of three samples with high rheumatoid factor concentrations were diluted with one human sample and evaluated.

No interference (based on acceptable recoveries) was observed for the following substances: biotin up to 100 ng/mL (osteocalcin 73.89 ng/mL), lipids up to 1500 mg/dL (osteocalcin 27.3 ng/mL), bilirubin up to 65 mg/dL (osteocalcin 39 ng/mL), and rheumatoid factor up to 2200 IU/mL (osteocalcin 20.0-252.1 ng/mL).

Various pharmaceutical compounds were spiked into a sample with osteocalcin concentration of approximately 50 ng/mL and tested by the Elecsys® N-MID Osteocalcin on the Elecsys® 2010 Immunoassay Analyzer. Each of the compounds were found to be non-interfering.

The specificity of the Elecsys® N-MID Osteocalcin Assay was determined on the Elecsys® 2010 Immunoassay Analyzer using samples spiked with potential cross-reactant compounds. No cross-reactivity was observed with β -Cross Laps at 15000 ng/mL and bone alkaline phosphatase at 140 U/L. Parathyroid hormone at 3918 pg/mL exhibited 5.4% cross-reactivity.

f. Assay cut-off:

See “Detection limit” above.

2. Comparison studies:

a. Method comparison with predicate device:

A comparison of Elecsys® N-MID Osteocalcin with a commercially available N-MID Osteocalcin test using 48 clinical samples (from 39 postmenopausal women and 9 men) gave the following correlations (ng/mL): $y = 1.307x + 2.0$, $r = 0.966$, $md(68) = 0.816$. Sample concentrations ranged between approximately 2.58 and 49.79 ng/mL.

b. Matrix comparison:

Twenty-five samples each drawn into serum, K₃-EDTA, and Li-Heparin plasma vacutainer tubes were compared to determine potential effects. Passing/Bablok and Least Squares were calculated, and the method comparison was found to be acceptable. Both the EDTA and heparin samples, when compared to serum, yielded slopes between 0.9-1.1.

3. Clinical studies:

a. Clinical Sensitivity:

Not applicable

b. Clinical specificity:

Not applicable

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

Elecsys® N-MID Osteocalcin (run on the Elecsys 2010) and a commercially available N-MID Osteocalcin were used to measure retrospective samples from 57 postmenopausal subjects participating in a clinical study involving two Calcitonin treatments over six months. Samples were taken from patients at weeks 0, 4, 12, and 24, yielding a total of 228 samples measured.

Sample concentrations ranged between approximately 9.19 and 93.38 ng/mL on the subject device. Passing/Bablok linear regression results were as follows: $y = 1.120x + 4.4$, $r = 0.922$, $md(68) = 1.337$.

4. Clinical cut-off:

Not applicable

5. Expected values/Reference range:

The reference ranges are test-dependent. Completed studies with Elecsys N-MID Osteocalcin have revealed the following ranges in ng/mL:

		N-MID Osteocalcin	
	Number	Median (ng/mL)	5-95 th Percentile
Healthy Women			
Premenopausal, >21 yrs			
Caucasian	133	18.5	9.7 – 35.1
Afro-American	160	16.3	7.6 – 30.7
Postmenopausal, w/o diagnosed osteoporosis			
Caucasian	141	17.5	7.3 – 37.8
Afro-American	160	18.1	8.4 – 38.5
Osteoporosis patients	103	29.1	17.3 – 48.6
Healthy Men			
30 – 50 yrs.			
Caucasian	130	22.9	10.2 – 36.7
Afro-American	151	18.3	8.4 – 33.6
51 – 70 yrs.			
Caucasian	117	18.5	10.8 – 31.1
Afro-American	117	17.6	9.9 – 35.6
>70 yrs.			
Caucasian	25	15.9	Sponsor notes that the percentile range isn't reliable for a sample size less than 110.
Afro-American	13	14.9	

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.