

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

A. 510(k) Number:

k070709

B. Purpose for Submission:

Add an indication for use for intra-operative use and include hemoglobin interference information for both the Elecsys PTH Test System and the Elecsys PTH STAT Test System.

C. Measurand:

Intact parathyroid hormone

D. Type of Test:

Quantitative, electro-chemiluminescence (ECLIA) assay

E. Applicant:

Roche Diagnostics

F. Proprietary and Established Names:

Roche Diagnostics Elecsys PTH Test System

Roche Diagnostics Elecsys PTH STAT Test System

G. Regulatory Information:

1. Regulation section:

21CFR 862.1545 – Parathyroid hormone test system

2. Classification:

Class II

3. Product code:

CEW

4. Panel:

Chemistry (75)

H. Intended Use:

1. Intended use(s):

See Indications for Use below

2. Indication(s) for use:

The Elecsys PTH Immunoassay is for the *in vitro* quantitative determination of intact parathyroid hormone in human serum and plasma for the differential diagnosis of hypercalcemia and hypocalcemia. The Elecsys PTH Immunoassay can be used intraoperatively.

The Elecsys PTH STAT Immunoassay is for the *in vitro* quantitative determination of intact parathyroid hormone in human serum and plasma for the differential diagnosis of hypercalcemia and hypocalcemia. The Elecsys PTH STAT Immunoassay can be used intraoperatively.

3. Special conditions for use statement(s):

For prescription use only.

The sponsor has the following limitations in the Elecsys PTH Immunoassay regarding the hemoglobin interference:

Do not analyze samples that show visible signs of hemolysis.

The assay is affected by hemolysis > or equal to 0.10 g/dL. For PTH results < 50 pg/mL, hemolysis (Hg < 0.0932 mmol/L or \geq 0.10 g/dL) can lead to a reduction by 3 to 5 pg/mL. For PTH results \geq 50 pg/mL, hemolysis (Hg < 0.0932 mmol/L or \geq 0.15 g/dL) affect the results by less than 10 percent.

The sponsor has the following limitations in the Elecsys PTH STAT Immunoassay regarding the hemoglobin interference:

Do not analyze samples that show visible signs of hemolysis.

The assay is affected by hemolysis > or equal to 0.25g/dL.

4. Special instrument requirements:

The Elecsys PTH Immunoassay can be used on the Elecsys 2010, MODULAR ANALYTICS E170, cobas e411 and cobas e601 analyzers.

The Elecsys PTH STAT Immunoassay can be used on the Elecsys 1010, 2010, cobas e411 analyzers.

I. Device Description:

Each cartridge of PTH or PTH STAT reagent consists of the following:

- Streptavidin-coated microparticles 0.72 mg/mL; preservative – in a 6.5 mL bottle with a transparent cap.
- Biotinylated monoclonal anti-PTH antibody (mouse) 2.3 mg/L; phosphate buffer 100 mmol/L, pH 7.0; preservative – in a 10 mL bottle with a gray cap.
- Monoclonal anti-PTH antibody (mouse) labeled with ruthenium complex 2.0 mg/L; phosphate buffer 100 mmol/L, pH 7.0; preservative – in a 10 mL bottle with a black cap.

J. Substantial Equivalence Information:

1. Predicate device name(s):

Elecsys PTH Test System and Elecsys PTH STAT Test System

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

k992680, k070391

3. Comparison with predicate:

Similarities and Differences between modified device and the predicate device)-k992680			
Item	Elecsys PTH assay Predicate device (k992680)	Elecsys PTH assay (18 minutes appl.) Modified device	Elecsys STAT PTH assay (9 minutes appl.) Modified device
Indications for Use	Immunoassay for the <i>in vitro</i> quantitative determination of intact parathyroid hormone in human serum and plasma for the differential diagnosis of hypercalcemia and hypocalcemia.	The Elecsys PTH Immunoassay is for the <i>in vitro</i> quantitative determination of intact parathyroid hormone in human serum and plasma for the differential diagnosis of hypercalcemia and hypocalcemia and can be used intraoperatively.	The Elecsys PTH STAT Immunoassay is for the <i>in vitro</i> quantitative determination of intact parathyroid hormone in human serum and plasma for the differential diagnosis of hypercalcemia and hypocalcemia and can be used intraoperatively.

Platform(s)	Elecsys 1010, 2010, Modular analytics E170, cobas e411 and cobas e601 analyzers.	Elecsys 2010, Modular analytics E170, cobas e411 and cobas e601 analyzers.	Elecsys 1010, 2010, cobas e411 analyzer
Assay Protocol	Sandwich assay	same	Same
Total assay duration	Elecsys 1010: 9 minute application Elecsys 2010, Modular analytics E170, cobas e411 and cobas e601 analyzers: 18 minute application	18 minute	9 minute
Detection Protocol	Electro-chemiluminescence	same	same
Sample Type	Human serum and plasma treated with K3-EDTA.	same	same
Calibrator	Elecsys PTH CalSet	Elecsys PTH CalSet	Elecsys PTH STAT CalSet
Measuring Range	1.20-5,000 pg/mL	same	same
Analytical Sensitivity	1.20 pg/mL	same	same
Analytical Specificity	No cross-reactivities were found for: Osteocalcin, PTH fragment 1-37, bone-specific alkaline phosphatase, and β -Crosslaps	same	same
Traceability	Standardized against a commercially available PTH test (RIA)	Standardized against a commercially available PTH test (RIA)	This method has been standardized against Elecsys PTH. This in turn was standardized against a commercially available PTH test (RIA)
Hook effect	No high dose hook effect at PTH concentrations up to 17,000 pg/mL	Same	Same
Limitations	Assay is unaffected by icterus (bilirubin <65 mg/dL), hemolysis (hemoglobin < 1.5 g/dL), lipemia (intralipid < 1500 mg/dL), Biotin <50 ng/mL, or RF < 1500 IU/mL. In patients receiving therapy with high biotin	Same for bilirubin, lipemia, biotin and RF. Labeling change to state: Do not analyze samples that show visible signs of hemolysis. Hemolysis \geq 0.10 g/dL will have an affect on the assay. For PTH results < 50 pg/mL,	Same for bilirubin, lipemia, biotin and RF. Labeling change to state: Do not analyze samples that show visible signs of hemolysis. Hemolysis \geq 0.25 g/dL will have an affect on the assay.

	dose (i.e > 5mg/day), no sample should be taken until at least 8 hrs after the last biotin administration.	hemolysis (Hg < 0.0932 mmol/L or ≥ 0.10 g/dL) can lead to a reduction by 3 to 5 pg/mL. For PTH results ≥ 50 pg/mL, hemolysis (Hg < 0.0932 mmol/L or ≥ 0.15 g/dL) affect the results by less than 10 percent.	
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K. Standard/Guidance Document Referenced (if applicable):

None referenced

L. Test Principle:

The Elecsys PTH 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. The assay time is 18 minutes.

The Elecsys PTH STAT 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. The assay time is 9 minutes.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

There were no changes to the technology or the assay reaction time. See performance characteristics established in k992680 and k070391.

b. Linearity/assay reportable range:

There were no changes to the technology or the assay reaction time. See performance characteristics established in k992680 and k070391.

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

There were no changes to the technology or the assay reaction time. See performance characteristics established in k992680 and k070391.

d. Detection limit:

There were no changes to the technology or the assay reaction time. See performance characteristics established in k992680 and k070391.

e. Analytical specificity:

Additional interference studies on hemoglobin were performed using the Elecsys PTH assay and Elecsys PTH STAT assay on the Elecsys 2010 analyzer.

For Elecsys PTH assay, 9 samples ranging from 13.6 to 854.0 pg/mL of PTH concentration were tested for the hemoglobin interference. The acceptance criterion is recovery $\pm 10\%$ of the initial value. The sponsor claimed that the assay is affected by a reduction of 3 to 5 pg/mL with hemolysis ≥ 0.10 g/dL for PTH < 50 pg/mL and assay is affected by less than 10 percent with hemolysis ≥ 0.15 g/dL for PTH ≥ 50 pg/mL.

For Elecsys PTH STAT assay, 6 samples ranging from 19.9 to 372.0 pg/mL of PTH concentration were tested for the hemoglobin interference. The acceptance criterion is recovery $\pm 10\%$ of the initial value. The sponsor claimed that the assay is affected by hemolysis ≥ 0.25 g/dL.

f. Assay cut-off:

Not Applicable

2. Comparison studies:

a. Method comparison with predicate device:

Performance characteristics were established in k992680

b. Matrix comparison:

Performance characteristics were established in k992680

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):

Published literature was provided to support the intraoperative claim^{1,2,3}. Studies were conducted on patients undergoing parathyroidectomy to evaluate the Elecsys PTH STAT assay (on Elecsys 1010 analyzer) and the Elecsys PTH assay (on Elecsys 2010 analyzer). The assay results were compared to clinical data and reported in the following peer reviewed journals:

1. Ohe, Monique Nakayama, Santos, Rodrigo Oliveira, Kunii, Ilda Shizue *et al.* "Usefulness of intra-operative PTH measurement in primary and secondary hyperparathyroidism: experience with 109 patients" *Arq Bras Endocrinol Metab.* 2006; 50 (5): 869-75.
2. Seehofer D, rayes N, Ulrich F, Muller C, Lang M, Neuhaus P, Steinmuller T. "Intra-operative measurement of intact parathyroid hormone in renal hyperparathyroidism by an inexpensive routine assay" *Langenbecks Arch Surg.* 2001; 386 (6): 440-3.
3. Seehofer D, Rayes N, Klupp J, Steinmuller T, Ulrich F, Muller C, Schindler R, Frei U, Neuhaus P. "Predictive value of intact parathyroid hormone measurement during surgery for renal hyperparathyroidism" *Langenbecks Arch Surg.* 2005; 390 (3): 222-9.

Study#1:

The study evaluated the Elecsys PTH assay for its intraoperative applicability in 109 patients with either a diagnosis of Primary Hyperparathyroidism (n=33), or Secondary Hyperparathyroidism due to renal disease (n=76). Of the latter cohort, 52 patients were on dialysis and 24 had a renal transplant. This study was conducted using the currently marketed Elecsys PTH STAT assay on the Elecsys 1010 instrument.

Blood samples were drawn after administration of anesthesia for baseline measurements and at 10 minutes and 20 minutes post resection of the parathyroid glands. The study used the generally accepted guidelines that a >50% decrease in PTH value from baseline suggests complete tumor removal. Of the 109 patients in the study group, 107 showed sufficient decrease by the second draw with an average decay of PTH of 79.2% of basal level within 10 minutes for the primary hyperparathyroid group, and 83.8% of basal level by 20 minutes. Among the renal patients the decay averaged 85.8% of basal level by 10 minutes and 87.2% by 20 minutes. Among the renal transplant patients the average decay from baseline was 87.6% in 10 minutes and 89.8% from baseline in 20 minutes.

Two patients did not show the sufficient 50% drop by the second draw at 20 minutes and therefore were classified correctly as unsuccessful surgeries. However, in both cases a second surgery was required and both surgeries were successful based on the required decay of 50% of the PTH value.

The assay met the generally accepted criterion of a >50% decrease from baseline (before incision) with complete tumor removal for 107 out of 109 patients initially and 2 out of 2 patients in follow-up surgeries.

Study #2:

The study was conducted using the currently marketed Elecsys PTH assay on the Elecsys 2010 instrument. In total, 34 patients underwent parathyroidectomy surgery for renal hyperparathyroidism, 31 of which underwent subtotal parathyroidectomy and 3 total parathyroidectomy. The study was divided into two parts. The first part

used the first 12 patients to compare the Elecsys PTH assay with the DPC Immulite assay and the Nichols Quick PTH assay. The second part of the study tested the ability of the Elecsys PTH assay to be used intraoperatively using the criterion of a decrease of 50% from baseline as the guideline for designation of a successful surgery, and combined the remaining 22 patients tested with only the Elecsys PTH assay giving a total of 34 patients evaluated.

The results of the comparisons are as follows: The Elecsys PTH assay was compared to the DPC Immulite assay and showed a correlation coefficient of 0.997 with no significant differences. The Elecsys PTH assay was then compared to the Nichols Quick assay using the same samples and showed a correlation coefficient of 0.987 with no significant differences.

For the 34 patients evaluated for successful parathyroidectomies based on PTH values, 33 patients showed >50% decrease from baseline levels at 5 minutes. The average level of decrease was 74% of the baseline level at 5 minutes post resection. At 15 minutes post resection, all patients showed >50% with an average level decrease of 82% of baseline level.

The assay met the generally accepted criterion of a >50% decrease from baseline (before incision) with complete tumor removal in 34 out of 34 patients in this study.

Study #3:

In this study, the investigators used two successive criteria of PTH decrease at the 15 minute time point. The first criterion was a PTH level at 15 minutes 150 pg/mL or less. If this was not achieved, the second criterion of a relative PTH decrease of 30% or less was used.

153 patients underwent parathyroid surgery for renal hyperparathyroidism and had blood drawn both pre- (before preparation of the parathyroid glands) and post (15 minutes after completion of the parathyroid resection) resections of the parathyroid glands to determine the applicability of the Elecsys PTH assay to predict a successful resection. 123 patients underwent subtotal parathyroidectomy and 13 patients underwent total parathyroidectomy during initial surgeries. Of the 153 patients, 24 had normal kidney function after transplant and 129 suffered from terminal renal failure. The samples were assayed on the Elecsys 2010 instrument and the per cent decrease was calculated from the baseline measurements.

The mean PTH decay from baseline for all patients was 81% at 15 minutes (862 pg/ml to 167 pg/mL). All 24 patients with compensated renal failure had PTH levels decrease >50% predicting successful operations. Of the 129 patients with terminal renal failure, the Elecsys PTH test showed 114 patients met both criteria. Of these, 108 had a true decline in PTH with no postoperative hyperparathyroidism, and 6 had a false decline in PTH with no persistent hyperparathyroidism. On the other hand, 15 patients did not meet both criteria and in whom only 3 parathyroid glands were found during surgery. Of these, 13 were classified as true failure to decline and 2 were classified as false failure to decline.

The assay met the generally accepted criterion of a >50% decrease from baseline with complete tumor removal.

4. Clinical cut-off:

Not Applicable

5. Expected values/Reference range:

Performance characteristics were established in k992680

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.