SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY TEMPLATE

A. 510(k) Number:

k101921

B. Purpose for Submission:

New device

C. Measurand:

Intact Parathyroid Hormone (iPTH)

D. Type of Test:

Quantitative, Enzyme-Linked Immunoassay (EIA)

E. Applicant:

Ortho-Clinical Diagnostics

F. Proprietary and Established Names:

1. VITROS Immunodiagnostics Products Intact PTH Reagent Pack
2. VITROS Immunodiagnostics Products Intact PTH Calibrators
3. VITROS Immunodiagnostics Products Range Verifiers
4. VITROS Immunodiagnostic Product Intact PTH Controls

G. Regulatory Information:

Product Code	Classification	Regulation Section	Panel
CEW	Class II	21 CFR 862.1545 Parathyroid Hormone Test System	Clinical Chemistry (75)
JIT	Class II	21 CFR 862.1150 Calibrator	Clinical Chemistry (75)
JJX	Class I, reserved	21 CFR 862.1660 Quality Control Material	Clinical Chemistry (75)

H. Intended Use:

1. Intended use(s):

Refer to indication for use below

2. Indication(s) for use:

   For the quantitative measurement of intact parathyroid hormone (iPTH) in human serum and plasma (EDTA or heparin) using the VITROS ECi/ECiQ Immunodiagnostic Systems and the VITROS 5600 Integrated System. Intact PTH is indicated to aid in the differential diagnosis of hyperparathyroidism, hypoparathyroidism, or hypercalcemia of malignancy and can be used intraoperatively.

3. Special conditions for use statement(s):

   For *in vitro* diagnostic use only

4. Special instrument requirements:

   VITROS ECi/ECiQ Immunodiagnostic Systems and VITROS 5600 Integrated System were used to conduct performance studies below.

I. Device Description:

1. VITROS Intact PTH Reagent Pack Contents:

   - 100 coated wells (streptavidin, binds >3 ng biotin/well)
   - 6.2 mL biotinylated antibody reagent (biotin-goat polyclonal anti-PTH, binds >20,000 pg PTH/mL) in buffer with bovine gamma globulin, bovine serum albumin, and antimicrobial agent
   - 8.4 mL conjugate reagent (HRP-goat polyclonal anti-PTH, binds >8,000 pg PTH/mL) in buffer with bovine serum albumin and antimicrobial agent

2. VITROS Intact PTH Calibrator Contents:

   - 3 sets of VITROS Intact PTH Calibrators 1, 2 and 3 (freeze-dried, synthetic PTH in buffer with bovine serum albumin and antimicrobial agent, reconstitution volume 1.0 mL); nominal values 0, 100 and 1500 pg/mL
   - Lot calibration card
   - Protocol card
   - 24 calibrator bar code labels (8 for each calibrator)

3. VITROS Intact PTH Range Verifier Contents:

   2 sets of VITROS Intact PTH Range Verifiers, low and high (freeze-dried, synthetic PTH in buffer with bovine serum and antimicrobial agent, reconstitution volume 1.0 mL); nominal values 0 and 4750 pg/mL

4. Control Pack Contents:

3 sets of VITROS Intact PTH Controls 1, 2 and 3 (freeze-dried, synthetic PTH in buffer with bovine serum and antimicrobial agent, reconstitution volume 1.0 mL)

J. Substantial Equivalence Information:

1. Predicate device name(s):

   Roche Diagnostics Corporation Elecsys Parathyroid Hormone Test System

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

   K070709

3. Comparison with predicate:

Items	VITROS® Intact PTH assay (Candidate Device)	Roche Elecsys Intact PTH assay (Predicate Device)
Similarity		
Intended Use	Same	It is intended for the in vitro quantitative determination of intact parathyroid hormone in human serum and plasma for the differential diagnosis of hypercalcemia and hypocalcemia, and can be used intraoperatively.
Tracer	Same	Enzyme labeled
Precision	Same	Total imprecision <10%
Measuring Range	3.4-5000 pg/mL	1.20-5000 pg/mL
Time to First Result	Same	18 minutes
Sample Type	Same	Serum and plasma (heparin and EDTA)
Difference		
Test Principle	Solid phase immunoassay	Sandwich assay
Antibody	Goat polyclonal	Mouse monoclonal
Sample Volume	80 µL	50 µl
Hook Effect	None up to 1,218,400 pg/mL	None up to 17,000 pg/mL
Normal Range	7.5–53.5 pg/mL	16.0-65 pg/mL
Calibrator		
Format	Same	Liquid
Levels	3	2
Matrix	Buffer with bovine serum and antimicrobial agent	Human serum with antimicrobial agent
Range Verifier		

Format	Same	Lyophilized
Levels	2 Low and High (<3.4 & 4750 pg/mL)	3 Low Medium and High
Matrix	Buffer with bovine serum antimicrobial agent	Human serum with antimicrobial agent
Control		
Format	Same	Lyophilized
Levels	3	3
Values	Approximately 25, 75 and 500 pg/mL	Approximately 20, 60 and 700 pg/mL
Matrix	Buffer with bovine serum and antimicrobial agent	Human serum with antimicrobial agent

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

- CLSI Guideline EP5-A2
- CLSI Guideline EP6-A
- CLSI Guideline EP7-A2
- CLSI Guideline EP9-A2
- CLSI Guideline EP17-A
- Standards Report for C28-A3: Defining, Establishing, and Verifying Reference Intervals in the Clinical Laboratory; Approved Guideline - Third Edition.
- Guidance for Industry and FDA Staff - Use of Symbols on Labels and in Labeling of In Vitro Diagnostic Devices Intended for Professional Use
- Points to Consider for Collection of Data in Support of In-Vitro Device Submissions for 510(k) Clearance
- Points to Consider for Review of Calibration and Quality Control Labeling for In Vitro Diagnostic Devices/Cover Letter dated 3/14/1996
- Guidance for Industry and FDA Staff - Assayed and Unassayed Quality Control Material

L. Test Principle:

An immunometric immunoassay technique is used, which involves the simultaneous reaction of PTH present in the sample with a biotinylated antibody (goat polyclonal anti-PTH39-84) and a horseradish peroxidase (HRP)-labeled antibody conjugate (goat polyclonal anti-PTH1-34). The antigen-antibody complex is captured by streptavidin on the wells. Unbound materials are removed by washing. The bound HRP conjugate is measured by a luminescent reaction. A reagent containing luminogenic substrates (a luminol derivative and a peracid salt) and an electron transfer agent is added to the wells. The HRP in the bound conjugate catalyzes the oxidation of the luminol derivative, producing light. The electron transfer agent (a substituted acetanilide) increases the level of light produced and prolongs its emission. The light signals are read by the system. The amount of HRP conjugate bound is directly proportional to the concentration of PTH present in the sample.

M. Performance Characteristics (if/when applicable):

1. <u>Analytical performance</u>:

a. Precision/Reproducibility:

Study Protocol:
Precision was evaluated following CLSI guideline EP5-A2. Two replicates of each of 3 freeze-dried control samples and 6 patient serum sample pools were tested on 2 separate runs per day for 20 different days. When spiking synthetic PTH into a patient sample pool, the spike solution made up no more than 5% of the total volume of the patient sample being spiked.

Precision Summary:

Sample description

Sample ID	Sample Description	iPTH Nominal Value (pg/mL)
SC-1	VITROS Control 1	30
SC-2	VITROS Control 2	80
SC-3	VITROS Control 3	500
PP-1	Endogenous Patient Serum Pool 1	15
PP-2	Endogenous Patient Serum Pool 2	40
PP-3	Spiked Patient Serum Pool 3	50
PP-4	Spiked Patient Serum Pool 4	100
PP-H	Spiked Patient Serum Pool 5	3000
PP-H2	Spiked Patient Serum Pool 6	4000

Precision

	Units = pg/mL								
	Mean	**Within-run***		**Within-calibration****		**Within-lab*****		**No.**	**No.**
System	**PTH Conc.**	**SD**	**CV (%)**	**SD**	**CV (%)**	**SD**	**CV (%)**	**Observ.**	**Days**
ECi/ECiQ system 1	25.8	0.545	2.1	1.120	4.3	1.200	4.7	80	20
	75.4	1.25	1.7	3.72	4.9	3.73	5.0	80	20
	499.5	8.32	1.7	17.7	3.5	18.3	3.7	80	20
	12.8	0.32	2.5	0.561	4.4	0.662	5.2	80	20
	42.4	3.14	7.4	3.52	8.3	4.06	9.6	80	20
	45.5	0.704	1.5	1.62	3.6	2.24	4.9	80	20
	105.8	1.37	1.3	3.17	3.0	3.74	3.5	80	20
	2974	41.4	1.4	64.0	2.2	104	3.5	80	20
	3593	65.7	1.8	86.4	2.4	134	3.7	80	20
ECi/ECiQ system 2	26.3	0.616	2.3	1.160	4.4	0.991	3.8	80	20
	76.7	1.39	1.8	2.42	3.2	2.31	3.0	80	20
	503.5	7.17	1.4	17.0	3.4	17.2	3.4	80	20
	13.6	0.357	2.6	0.611	4.5	0.553	4.1	80	20
	47.2	0.745	1.6	1.27	2.7	1.26	2.7	80	20
	49.4	0.773	1.6	1.68	3.4	1.71	3.5	80	20
	112	1.82	1.6	3.04	2.7	6.16	5.5	80	20
	3246	32.9	1.0	64.8	2.0	92.4	2.8	80	20
	3891	56.2	1.4	101	2.6	254	6.5	80	20
5600	27.6	0.588	2.1	1.93	7.0	2.09	7.6	80	20
	78.1	1.72	2.2	4.04	5.2	4.50	5.8	80	20
	505.3	8.13	1.6	18.3	3.6	20.0	4.0	80	20

System	Units = pg/mL								
	Mean PTH Conc.	Within-run*		Within-calibration**		Within-lab***		No. Observ.	No. Days
		SD	CV (%)	SD	CV (%)	SD	CV (%)		
	14.2	0.257	1.8	0.863	6.1	0.928	6.5	80	20
	47.6	0.537	1.1	1.82	3.8	2.54	5.3	80	20
	51.7	0.745	1.4	1.55	3.0	2.57	5.0	80	20
	116.4	1.49	1.3	3.00	2.6	5.63	4.8	80	20
	3155	28.8	0.9	49.8	1.6	97.5	3.1	80	20
	3782	46.2	1.2	92.6	2.4	222	5.9	80	20

* Within-run (repeatability). Between Duplicate precision averaged over all runs

** Within-calibration. Total precision with weighted components of within-run, between–run and between-day variation.

*** Within-lab. A measure of the effect of recalibration on total precision, calculated within reagent lot, using data from at least 4 calibrations

b. Linearity/assay reportable range:

Study Protocol:
Linearity was evaluated following CLSI guideline EP6-A on 2 VITROS ECi/ECiQ Immunodiagnostic Systems and 1 VITROS 5600 Integrated System. Altered serum pool samples were used for the studies. The low pool was an endogenous serum sample stripped for PTH and had an estimated PTH concentration of 2.0 pg/mL. The high pool was either an endogenous patient pool (estimated PTH concentration 700 pg/mL) or a patient pool spiked with synthetic PTH (estimated PTH concentration 5500 pg/mL). For the whole range study, the spiked high serum pool and the low serum pool were mixed to give 11 additional pools of intermediate concentrations spanning the range of 2.0 - 5500 pg/mL. For the clinical relevant range study, the endogenous patient pool and the low serum pool were mixed to give 11 additional pools of intermediate concentrations spanning the range of 2.0 - 700 pg/mL.

Result Summary:
Statistical evaluations for both studies using polynomial regression indicate that the data were best fitted by a 3rd order regression with less than 10% bias from the linear fitted results.

Conclusion:
Based on the linearity results, the sponsor claimed that the assay is linear from 3.4 pg/mL to 5000 pg/mL.

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

Traceability:

Calibration of the VITROS Intact PTH test is traceable to in-house reference calibrators, which value have been assigned to correlate to the predicate device, the Roche Elecsys PTH.

Stability:

Real-time testing was conducted. The stability study protocol and the acceptance criteria have been reviewed and found to be acceptable. The study results support the stability claims summarized in the below table.

Close-Vial and Open-Vial Stability

Item	Storage Conditions		Claimed Stability
Reagent Packs	Close-Vial	2-8°C	26 weeks
	Open-Vial	On system	8 weeks
	Open-Vial	2-8°C	8 weeks
Calibrators	Close-Vial	2-8°C	26 weeks
	Open-Reconstituted	2-8°C	1 day
	Open-Reconstituted	-20°C	8 weeks
Range Verifiers	Close-Vial	2-8°C	26 weeks
	Open-Reconstituted	2-8°C	1 day
	Open-Reconstituted	-20°C	5 days
Controls	Close-Vial	2-8°C	26 weeks
	Open-Reconstituted	2-8°C	1 day
	Open-Reconstituted	-20°C	4 weeks

Calibration Interval:

Stability across a 28 day calibration interval was assessed by calculating the percentage bias of the precision samples on each day from the result obtained for that precision samples from the calibration on the first day. The results support the product claim of a 28-day calibration interval.

Value Assignment:

- Calibrators: The in-house reference calibrators, which values have been assigned to correlate to the predicate device, were used to generate the master calibration curve. The lot specific calibrator value was determined as the mean of 20 assays per master lot, using 2 VITROS ECi/ECiQ Immunodiagnostic Systems and 1 VITROS 5600 Integrated System.
- Range Verifiers: The acceptance criterion for the Low Range Verifier is <3.4 pg/mL, for the High Range Verifier is 4000-5500 pg/mL.
- Controls: The target values are 25, 75 and 500 pg/mL. The lot specific range was assigned as mean ± 3 SD. The Mean and SD was calculated from 32 test results (2 tests per run, 5 or 6 runs per kit lot, using 3 kit lots and at least 2 VITROS systems).

d. Detection limit:

Study Protocol:

Limit of Blank (LoB), Limit of Detection (LoD) and Limit of Quantitation (LoQ) were determined following CLSI guideline EP17-A on 2 VITROS ECi/ECiQ Immunodiagnostic Systems and 1 VITROS 5600 Integrated System.

For LoB determination, 10 replicates of the zero calibrator buffer were run on 2 occasions per day for 5 days, assessed from three calibrations (days 1, 3 and 5) – giving 100 determinations in total.

For LoD determination, 10 replicates of each of five LoD pools were run on 2 occasions per day for 5 days across three calibrations (days 1, 3 and 5) – giving 100 determinations of each pool in total. The five LoD pools were made by diluting an endogenous patient pool in the zero calibrator buffer used for the Limit of Blank to give estimated iPTH concentrations of 2.5, 3.0, 3.5, 4.0 and 4.5pg/mL.

For LoQ determination, two additional pools with estimated iPTH concentrations of 5.0 and 5.5 pg/mL were included in addition to the 5 pools used in the LoD study. The level of imprecision used to accept the LoQ was within 20%.

Result Summary:

The following detection limit claims were made based on the worst case results:

LoB	LoD	LoQ
1.2 pg/mL	2.8 pg/mL	3.4 pg/mL

e. Analytical specificity:

- Interference

  Study Protocol:
  The sponsor evaluated the effect of the interfering substances on 2 VITROS ECi/ECiQ Immunodiagnostic Systems and 1 VITROS 5600 Integrated System using a patient serum pool with endogenous PTH between 20 and 80 pg/mL. For each substance, two aliquots of this pool were thawed, one spiked with the test substance up to the maximum level shown below, and the other spiked with the solvent (control). The PTH results (mean of 12 replicates) of the paired pools were compared and % interference was calculated using the following equation:

  $$\% \text{ Interference} = \frac{(\text{Mean of test substance pool}) - (\text{Mean of "control" pool})}{\text{Mean of "control" pool}} \times 100$$

  Result Summary:
  Based on the sponsor-defined interference limit of ± 10%, the following claims were

made:

- ❖ The below compounds at the indicated concentration do not cause significant interference with the assay.

Compound	Concentration up to
Azide (sodium)	20 mg/dL
Bilirubin	20 mg/dL
Biotin	500 ng/dL
Dipyrone	100 mg/dL
Hemoglobin (hemolysate)*	161 mg/dL
Intralipid	850 mg/dL
Triolein	2500 mg/dL

- ❖ Interference by Hemoglobin at >=250 mg/dL is stated in "Limitations of the Procedure" in the labeling. Additionally, the sponsor added "Do not use hemolyzed specimens." under section "Specimens Not Recommended".

- ❖ No interference is seen with Rheumatoid Factor (RF concentration up to 4935 IU/mL) or HAMA samples (HAMA concentration up to 1825 ng/mL) or with HAMA spiked endogenous samples (HAMA concentration up to 2000 ng/mL).

- Cross-Reactivity

Study Protocol:
The sponsor evaluated cross-reactivity by using the zero calibrator buffer as the test matrix. This calibrator had a PTH concentration below the Limit of Blank. Three determinations of each cross-reactant and corresponding "control" were carried out with each of the two reagent lots using 3 VITROS Immunodiagnostic Systems (2 VITROS ECi/ECiQ Immunodiagnostic Systems and 1 VITROS 5600 Integrated System). % Cross-reactivity was calculated using the following the equation:

$$\% \text{ Cross-reactivity} = \frac{\text{Mean iPTH of the Cross-Reactant pool}}{\text{Concentration of Cross-Reactant}} \times 100$$

Result Summary:
Based on the sponsor-defined % Cross-reactivity limit of 0.01%, none of the tested substances (except PTH 7-84) at the indicated concentration would cross react significantly with the proposed assay.

Cross-reactant Tested	**Concentration**	**Mean PTH Conc. of Cross-reactant Pool**	**% Cross-reactivity**
		Units pg/mL	
Bone Specific alkaline phosphatase	7.5ng/mL	<3.4	NA*
Calcitonin	10,000 pg/mL	<3.4	NA*
ß-Cross laps	1 ng/mL	<3.4	NA*

Osteocalcin	50 ng/mL	<3.4	NA*
PTH 1–34	100,000 pg/mL	3.9	0.00
PTH 39–68	100,000 pg/mL	4.8	0.00
PTH 39–84	100,000 pg/mL	14.8	0.01
PTH 44–68	100,000 pg/mL	4.5	0.00
PTH 53–84	100,000 pg/mL	4.8	0.00
PTH 7-84	1,000 pg/mL	925.2	92.5

*NA = Not Applicable. Concentration was below the measuring range of the test.

f. Assay cut-off:

Not applicable.

2. Comparison studies:

a. Method comparison with predicate device:

Study Protocol:

A total of 456 patient serum samples from a commercial vendor were used in the method comparison studies. These samples cover a variety of clinical categories (Hypoparathyroidism, Hyperparathyroidism, Chronic Renal Failures, Hypercalcemia of Malignancies and random donors). To cover the upper measuring range of the proposed iPTH assay, 21 patient samples were spiked with different concentrations of synthetic iPTH with target concentrations between 200 pg/ml and 4750 pg/ml. Regression analysis was performed between each of the VITROS systems (5600 and ECi/ECiQ) and the Predicate.

Result Summary:
The Result of Passing Bablok Regression analysis is summarized in the below Table.

Instrument	N	Range (pg/mL)	Slope	Intercept	r
VITROS 5600 vs. Predicate	412	3.5-4556	1.01	+0.5	0.99
VITROS ECi/ECiQ vs. Predicate	204	4.0-4751	1.05	-1.33	0.99

Conclusion:
Based on the regression analysis result, the sponsor claimed equivalency to the predicate assay.

b. Matrix comparison:

Study Protocol:
The matrix effect of various blood collection tubes on fresh and stored serum or plasma samples were evaluated. 40 apparently healthy volunteers were enrolled in the study. For each study participant, blood was collected into each of the following tube types: serum-plain glass, serum-plastic, lithium heparin plasma plastic, sodium heparin plasma plastic,

EDTA plasma plastic, SST plastic and lithium heparin PST plastic. To cover the entire measuring range of the assay, an additional 10 test samples were created by spiking different volumes of a synthetic PTH stock solution into 500 µl of serum or plasma samples from 10 patients. Aliquots from 40 endogenous samples and 10 spiked samples were made from the respective primary tubes and tested for various storage conditions.

Differences in PTH values (mean of three singlet determinations on VITROS 5600 and ECi/ECiQ system 1 and 2) between serum (glass) and each of the other six collection tubes on freshly collected samples were evaluated using Bias plots and correlation graphs.

To evaluate the effect of various storage conditions on PTH, % Difference was calculated using the following equation:

$$\% \text{ Difference} = \frac{\text{Test Condition - Baseline Condition}}{\text{Baseline Condition}} \times 100$$

Result Summary:

1. Matrix effect on freshly collected sample for PTH range 20-4876 pg/mL

Tube Y	Tube X	Slope	Intercept	r	PTH range
Serum Plastic	Serum Glass	1.05	1.38	0.999	20-4876 mg/dL
Lithium heparin plasma plastic	Serum Glass	1.04	0.42	0.998	
Lithium heparin PST plasma plastic	Serum Glass	1.03	4.61	0.993	
Sodium heparin plasma plastic	Serum Glass	1.03	-4.09	0.994	
EDTA plasma plastic	Serum Glass	0.97	10.01	0.999	
SST plastic	Serum Glass	1.02	-9.45	0.998	

2. To demonstrate equivalence at the low dose iPTH range (3.4 – 20 pg/ml), the sponsor presented data from the method comparison study showing that the 95% confidence intervals for EDTA plasma and serum samples overlap, and there is no statistical difference between the two collection devices, see below:

Sample Type	N	Slope (95% CI)	Intercept (95% CI)	Range of Samples (pg/mL)
Serum	134	0.97 (0.88 to 1.07)	-0.16 (-1.66 to 1.25)	6.4 to 18.4
Plasma	34	1.04 (0.78 to 1.36)	1.26 (-0.80 to 3.12)	3.6 to 20.5

3. To address the concern regarding performance in serum separator tubes and other collection devices at the low end of the measuring range, the sponsor has conducted an additional study on twenty samples (see below table). This data suggests that the position of the intercept on the y-axis can be significantly increased by including sample values up to the top of the measuring range. The study also suggests that intercepts of +9.0 or +10.0 (seen in the original study) are not expected when assessing sample data around the normal range:

Sample Types	n	Slope	Intercept	r	Sample Range (pg/mL)
Glass vs. EDTA	20	1.01	-0.40	0.997	28.10-103.13
Glass vs. Heparin	20	1.04	-1.01	0.997	28.10-103.13
Glass vs. Lithium	20	1.05	-0.29	0.994	28.10-103.13
Glass vs. SST	20	1.01	-1.36	0.995	18.30-66.60

4. In addition to the data presented above, the sponsor has also evaluated the matrix effect on sample stability:

	% Difference from fresh sample					
	2-8 °C				-20 °C	
Collection Tube	1 Day	2 Days	5 Days	7 Days	4 Weeks	2X F/T*
Serum glass	-11%	-14%	-23%	-27%	-15%	-14%
Serum plastic	-11%	-14%	-25%	-33%	-5%	-4%
Lithium Heparin	-9%	-8%	-13%	-17%	-1%	-6%
Sodium Heparin	-9%	-9%	-14%	-16%	-2%	-2%
EDTA	-10%	-9%	-10%	-12%	-8%	18%
SST Plastic	-12%	-16%	-27%	-34%	0%	-10%
Lithium Heparin PST	-10%	-9%	-13%	-17%	-5%	3%

* F/T, Freeze-and-Throw

Conclusion: Based on the study results, the sponsor has included the following precautions in the Instructions for Use for collection devices:

Special Precautions
IMPORTANT: Intact PTH is labile and susceptible to fragmentation. Correct handling of patient samples is necessary to ensure that the PTH molecule remains intact. The degree of fragmentation will depend on both time and temperature of storage.

Specimen Collection, Preparation and Storage

Specimen types should not be used interchangeably during the serial monitoring of an individual patient as measured concentrations may vary slightly between sample types.

Certain collection devices have been reported to affect other analytes and tests. Owing to the variety of specimen collection devices available, Ortho Clinical Diagnostics is unable to provide a definitive statement on the performance of its products with these devices. Confirm that your collection devices are compatible with this test. Storage of samples collected and stored in serum separator tubes for more than one day may result in a decrease in concentration of up to 20%.

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):

The sponsor evaluated the proposed iPTH assay for its intraoperative applicability in 39 patients who underwent parathyroid surgery. Samples from 20 patients were sourced in the U.S.; samples from 19 patients were sourced in the E.U. The number of samples per patient was not pre-established but was decided during surgery and based on the observed decrease in PTH concentration. The study used the generally accepted guidelines that a >50% decrease in PTH value from baseline suggests complete tumor removal.

31 out of 39 sample series showed a post operative drop of >50% in the intact PTH values. For all 39 samples the VITROS Intact PTH assay results were similar to the reference method values.

4. Clinical cut-off**:**

Not applicable

5. Expected values/Reference range:

240 archived serum samples with normal Calcium, TSH, Creatinine and Vitamin D values were used to determine the reference range of this assay. These samples were obtained from commercial vendors or hospital laboratories sourced in the U.S. to represent a US population.

The samples were assayed across the instrument platforms using two reagent lots as shown below. The reference interval is the central 95% of the iPTH results.

Instrument	Reagent Lot	Number of Samples	Reference Interval
VITROS ECi/ECiQ System 1	7	60	7.5 to 53.5 pg/mL
VITROS ECi/ECiQ System 2	8	60	
VITROS 5600 System 1	7	60	

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.