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

A. 510(k) Number:

k153375

B. Purpose for Submission:

New Device

C. Measurand:

Total 25-hydroxyvitamin D (25-OH vitamin D)

D. Type of Test:

Quantitative chemiluminescent microparticle immunoassay

E. Applicant:

Abbott Laboratories

F. Proprietary and Established Names:

ARCHITECT 25-OH Vitamin D 5P02
ARCHITECT 25-OH Vitamin D 5P02 Calibrators
ARCHITECT 25-OH Vitamin D 5P02 Controls

G. Regulatory Information:

1. Regulation section:

   21 CFR 862.1825, Vitamin D Test System

   21 CFR 862.1150, Calibrator

   21 CFR 862.1660, Quality Control Material (assayed and unassayed)

2. Classification:

   Class II

   Class II

Class I, reserved

3. Product code:

   MRG-Vitamin D Test System

   JIT-Calibrator, secondary

   JJX- Quality Control Material

4. Panel:

   Clinical Chemistry (75)

H. Intended Use:

1. Intended use(s):

   See indications for use below.

2. Indication(s) for use:
   The ARCHITECT 25-OH Vitamin D assay is a chemiluminescent microparticle immunoassay (CMIA) for the quantitative determination of 25-hydroxyvitamin D (25-OH vitamin D) in human serum and plasma. The ARCHITECT 25-OH Vitamin D assay is to be used as an aid in the assessment of vitamin D sufficiency.

   The ARCHITECT 25-OH Vitamin D Calibrators are for the calibration of the ARCHITECT i System when used for the quantitative determination of 25-hydroxyvitamin D (25-OH vitamin D) in human serum and plasma.

   The ARCHITECT 25-OH Vitamin D Controls are for the estimation of test precision and the detection of systematic analytical deviations of the ARCHITECT i System when used for the quantitative determination of 25-hydroxyvitamin D (25-OH vitamin D) in human serum and plasma.

3. Special conditions for use statement(s):

   For prescription use only

4. Special instrument requirements:

   Abbott ARCHITECT i2000SR

I. Device Description:

1. The ARCHITECT 25-OH Vitamin D 5P02 reagent kit contains:
   - Microparticles: Anti-vitamin D IgG (rabbit monoclonal) coated microparticles in MES Buffer. Minimum concentration: 0.04% solids. Preservative: ProClin 300.
   - Conjugate: Acridinium-labeled vitamin D in MES Buffer and surfactant. Minimum concentration: 12 ng/mL labeled vitamin D. Preservative: Sodium Azide.
   - Assay Diluent: Citrate buffer with EDTA, Methanol, 8-anilino-1-naphthalenesulfonic acid (ANSA), and surfactant. Preservative: ProClin 300.

2. The ARCHITECT 25-OH Vitamin D 5P02 Calibrators contain:
   Six bottles (4.0 mL each) of assigned concentrations of 25-OH Vitamin D in human serum and PBS buffer with sodium azide and ProClin 950 as preservatives. Calibrator concentrations (A-F) are 0, 4.0, 10.0, 30.0, 75.0, and 160 ng/mL.

3. The ARCHITECT 25-OH Vitamin D 5P02 Controls contain:
   3 bottles (8.0 mL each) of Low, Medium, and High Controls that contain 25-OH vitamin D prepared in PBS buffer with human serum with sodium azide and ProClin 950 as preservatives.

ARCHITECT 25-OH Vitamin D 5P02 Control	Target concentration (ng/mL)	Control range (ng/mL)
Low	20.0	14.0-26.0
Medium	40.0	28.0-52.0
High	75.0	52.4- 97.5

The calibrator and control materials have been tested by FDA-approved methods and found negative for the presence of HBsAg, antibody to HIV- 1/2 and HCV.

J. Substantial Equivalence Information:

1. Predicate device name(s):

   ARCHITECT 25-OH Vitamin D

   ARCHITECT 25-OH Vitamin D Calibrators

   ARCHITECT 25-OH Vitamin D Controls

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

   k110619

3. Comparison with predicate:

Similarities and differences for assay		
Item	Candidate device ARCHITECT 25-OH Vitamin D 5P02 (k153375)	Predicate device ARCHITECT 25-OH Vitamin D (k110619)
Intended Use	The ARCHITECT 25-OH Vitamin D assay is a chemiluminescent microparticle immunoassay (CMIA) for the quantitative determination of 25-hydroxyvitamin D (25-OH vitamin D) in human serum and plasma. The ARCHITECT 25-OH Vitamin D assay is to be used as an aid in the assessment of vitamin D sufficiency.	Same
Sample Type	Serum and EDTA, Sodium Heparin, Lithium Heparin plasma	Serum and Sodium Heparin, Lithium Heparin plasma
Assay Methodology	chemiluminescent immunoassay	Same
Assay Range	3.4 – 155.9 ng/mL	13.0-96.0 ng/mL
Traceability/ Standardization	Traceable to the ID-LC/MS/MS 25 (OH) vitamin D reference measurement procedure (University of Ghent) via patient sample correlation.	Traceable to an Internal reference standard
Reference range	6.2 ng/mL to 53.2 ng/mL	<13.0- 47.8 ng/mL

Similarities and Differences for Calibrators		
Item	Candidate device ARCHITECT 25-OH Vitamin D 5P02 Calibrators (k153375)	Predicate device ARCHITECT 25-OH Vitamin D Calibrators (k110619)
Intended Use	For the calibration of the ARCHITECT i System when used for the quantitative determination of 25-hydroxyvitamin D (25-OH vitamin D) in human serum and plasma.	Same
Matrix	Human Serum and PBS buffer	Same
Format	Liquid	Same
Levels	Approximately 0-160 ng/mL (0, 4.0, 10,0, 30.0, 75.0 and 160.0 ng/mL)	Same

Similarities and Differences for Calibrators		
Item	Candidate device ARCHITECT 25-OH Vitamin D 5P02 Calibrators (k153375)	Predicate device ARCHITECT 25-OH Vitamin D Calibrators (k110619)
Traceability/ Standardization	Standardized against NIST SRM 2972 and traceable to the ID-LC/MS/MS 25 (OH) vitamin D reference measurement procedure (University of Ghent) via patient sample correlation.	Traceable to an Internal reference standard

Similarities and Differences for Controls		
Item	Candidate device ARCHITECT 25-OH Vitamin D 5P02 Controls (k153375)	Predicate device ARCHITECT 25-OH Vitamin D Controls (k110619)
Intended Use	The ARCHITECT 25-OH Vitamin D Controls are for the estimation of test precision and the detection of systematic analytical deviations of the ARCHITECT I System when used for the quantitative determination of 25-hydroxyvitamin D (25-OH vitamin D) in human serum and plasma.	Same
Matrix	Human Serum and PBS buffer	25-OH Vitamin D in PBS buffer with heat inactivated horse serum.
Format	Liquid	Same
Levels	Low: 20.0 ng/mL Medium: 40.0 ng/mL High: 75.0 ng/mL	Same

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

CLSI EP5-A2: Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline – Second Edition

CLSI EP6-A: Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach; Approved Guideline

CLSI C24-A3: Statistical Quality Control for Quantitative Measurement Procedures: Principles and Definitions; Approved Guideline

CLSI C28-A3c: Establishing, and Verifying Reference Intervals in the Clinical Laboratory; Approved Guideline – Third Edition

CLSI EP7-A2: Interference Testing in Clinical Chemistry; Approved Guideline.

CLSI EP09-A3: Measurement Procedure Comparison and Bias Estimation Using Patient Samples; Approved Guideline

CLSI EP25-A: Evaluation of Stability of In Vitro Diagnostic Reagents; Approved Guideline.

L. Test Principle:

The ARCHITECT 25-OH Vitamin D 5P02 assay is a delayed one-step immunoassay including a sample pre-treatment for the quantitative determination of vitamin D in human serum and plasma using CMIA technology with flexible assay protocols, referred to as Chemiflex. Sample and pre-treatment reagents are combined. An aliquot of the pre−treated sample is combined with assay diluent and paramagnetic anti−vitamin D coated microparticles to create a reaction mixture. Vitamin D present in the sample binds to anti-vitamin D coated microparticles. After incubation a biotinylated vitamin D anti-Biotin acridinium-labeled conjugate complex is added to the reaction mixture and binds to unoccupied binding sites of the anti-vitamin D coated microparticles. After washing, pre-trigger and trigger solutions are added to the reaction mixture. The resulting chemiluminescent reaction is measured as relative light units (RLUs). An indirect relationship exists between the amount of vitamin D in the sample and the RLUs detected by the ARCHITECT i System optics.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

   a. *Precision/Reproducibility:*

   A study was performed in accordance with CLSI EP5-A2 in which seven (7) serum samples (ranging from 5.0 ng/mL to 152.6 ng/mL) and three control levels (20.0, 40.0, and 75.0 ng/mL) were assayed in duplicate in two runs per day for 20 non-consecutive days on two i2000SR analyzers using three reagent lots for a total of 360 results per sample (120 results per analyzer per sample). Each analyzer/reagent lot produced similar precision results. The within-run and total precision results are summarized in the table below using one representative lot of reagents:

   Representative lot precision:

		Within-run			Total	
	N	Mean (ng/mL)	SD	CV%	SD	CV%
Serum 1	119	5.0	0.25	5.1	0.35	7.1
Serum 2	120	9.5	0.26	2.8	0.40	4.2
Serum 3	119	20.6	0.44	2.1	0.70	3.4
Serum 4	119	30.1	0.59	1.8	0.69	2.3
Serum 5	120	72.2	1.66	3.3	2.51	3.5
Serum 6	120	109.1	3.29	3.0	4.55	4.2
Serum 7	120	158.1	6.2	3.9	7.31	4.6

		Within-run			Total	
	N	Mean (ng/mL)	SD	CV%	SD	CV%
Control 1	120	20.2	0.46	2.3	0.60	3.0
Control 2	120	40.2	0.83	2.1	1.25	3.1
Control 3	120	76.7	1.70	2.2	2.47	3.2

The combined lot precision is summarized in the table below:

ID	N=360	Within run		Between run		Between day		Between lot		Total	
	Mean (ng/mL)	SD	CV %	SD	CV %	SD	CV %	SD	CV %	SD	CV %
S1	5.3	0.24	4.5	0.11	2.1	0.26	4.8	0.05	0.9	0.37	6.9
S2	10.0	0.28	2.8	0.13	1.3	0.29	2.9	0.07	0.7	0.42	4.2
S3	21.1	0.41	1.9	0.22	1.1	0.49	2.3	0.26	1.2	0.67	3.2
S4	30.5	0.63	2.1	0.47	1.6	0.51	1.7	0.49	1.6	0.94	3.1
S5	72.4	1.53	2.1	0.61	0.8	1.56	2.2	1.44	2.0	2.26	3.1
S6	110.6	2.97	2.7	0.00	0.0	3.09	2.8	2.96	2.7	4.29	3.9
S7	153.1	5.91	3.9	1.84	1.2	3.10	2.0	4.65	3.0	6.93	4.5
C1	20.6	0.44	2.1	0.17	0.8	0.49	2.4	0.19	0.9	0.68	3.3
C2	40.6	0.82	2.0	0.38	0.9	0.84	2.1	0.50	1.2	1.23	3.0
C3	77.3	1.81	2.3	0.53	0.7	2.00	2.6	0.90	0.7	2.75	3.6

b. Linearity/assay reportable range:

Linearity was evaluated based on CLSI EP-6A, Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach. A linearity sample set was prepared by diluting a serum sample with a high 25-OH vitamin D concentration with a serum sample with a low 25-OH vitamin D concentration to obtain twelve (12) concentration levels across the measuring range of the candidate assay. Samples were run in replicates of 4 on one i2000SR analyzer using one reagent lot. The weighted Deming linear regression of the observed mean concentrations versus the expected concentration was calculated and yielded the following linear regression equation: $y = 0.9435x + 0.4$ ng/mL, $r = 1.00$, Test range: 3.4-160.3 ng/mL

The summary of observed concentrations versus the expected concentration is provided in the table below.

Mean observed concentration (ng/mL)	Expected concentration (ng/mL)	Difference (ng/mL)	% Difference
160.3	160.3	0.0	0.0
142.2	150.5	-8.3	-5.5
134.0	140.7	-6.6	-4.7
113.9	121.1	-7.1	-5.9
96.2	101.4	-5.3	-5.2
76.1	81.8	-5.7	-7.0
59.1	62.2	-3.1	-5.0
39.3	42.6	-3.3	-7.7
22.7	23.0	-0.3	-1.4
13.6	13.2	0.4	2.8
8.1	8.3	-0.2	-1.8
3.4	3.4	0.0	0.0

The results of the linearity study support the sponsor's claim that the assay is linear from 3.4 -155.9 ng/mL.

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

Standardization and Traceability

The ARCHITECT 25-OH Vitamin D Assay was originally cleared under 510(k) k110619. Abbott has modified the assay by standardizing the cleared vitamin D assay in accordance with the Vitamin D Standardization Certification Program (VDSCP). The VDSCP is an international collaborative effort to standardize the laboratory measurement of serum 25-OH vitamin D This collaboration involves the coordinated efforts of the National Institutes of Health, Office of Dietary Supplements (ODS), the Centers for Disease Control and Prevention (CDC), the National Institutes for Standards and Technology (NIST), Ghent University, and other institutions. Please refer to http://ods.od.nih.gov/Research/VitaminD.aspx for more information on the VDSCP program.

To achieve standardization against the VDSP recognized Reference Measurement Procedure (RMP), the ARCHITECT 25-OH Vitamin D 5P02 assay master calibration parameters were aligned to the CDC VDSP by using 129 human serum samples from the CDC VSDP program which were value assigned by the RMP and traceable to NIST SRM2972.

Calibrator traceability and value assignment

This assay is traceable to the isotope dilution-liquid chromatography/tandem mass spectrometry (ID-LC-/MS/MS) 25-OH Vitamin D Reference Method Procedure (RMP) that is traceable to the National Institute of Standards and Technology (NIST) Standard Reference Material (SRM) 2972. The calibrator traceability and value assignment are prepared according to an internal procedure.

The values of the primary reference materials were assigned to align with CDC VDSP recognized RMP, Ghent University ID-LC-MS/MS. The values of the secondary reference material were assigned using the ARCHITECT analyzer with the primary reference materials as calibrators. The values of the ARCHITECT Vitamin D 5P02 Calibrators supplied to the user, are assigned using the ARCHITECT analyzer with the secondary reference materials as calibrators. The ARCHITECT 25-OH Vitamin D 5P02 Calibrator target values are listed below:

Calibrator A: 0 ng/mL
Calibrator B: 4.0 ng/mL
Calibrator C: 10.0 ng/mL
Calibrator D: 30.0 ng/mL
Calibrator E: 75.0 ng/mL
Calibrator F: 160.0ng/mL

The ARCHITECT 25-OH Vitamin D 5P02 assay (candidate device) has passed the certification process for the CDC VDSP and a certificate has been provided by the CDC. Please see http://www.cdc.gov/labstandards/hs.html for more information on the CDC VDSCP certification program.

Control value assignment:

The ARCHITECT 25-OH Vitamin D 5P02 low, medium, and high controls are prepared gravimetrically, targeting 20.0, 40.0, and 75.0 ng/mL, respectively. The controls are run in replicates of 22 on one ARCHITECT iSystem analyzer to verify the target concentrations.

ARCHITECT 25-OH Vitamin D 5P02 Control	Target concentration (ng/mL)	Control range (ng/mL)
Low	20.0	14.0-26.0
Medium	40.0	28.0-52.0
High	75.0	52.4- 97.5

Stability

The calibrator and control shelf-life and open-vial stability testing protocols and acceptance criteria were reviewed and found to be acceptable. The stability studies

support the claim that the ARCHITECT 25-OH Vitamin D 5P02 Calibrators are stable for 8 months when stored un-opened at 2-8 °C and are stable for 30 days after opening at 2-8° C. The ARCHITECT 25-OH Vitamin D 5P02 Controls are stable for 8 months when stored un-opened at 2-8 °C and are stable for 30 days after opening at 2-8° C. Real-time studies are on-going and are scheduled to continue for a total of 18 months.

d. Detection limit:

The Limit of Blank (LoB), Limit of Detection (LoD) and Limit of Quantification (LoQ) studies were performed according to CLSI EP-17A2.

To establish the Limit of Blank (LoB), four blank samples (human serum based calibrator 1) were assayed 60 times using two reagent lots over multiple days on two analyzers. The Limit of Blank was the value at the 95th percentile and was determined to be 1.6 ng/mL.

To determine the Limit of Detection (LoD), 14 low level samples, with concentrations in the range from 0.5 to 3.5 ng/mL, were measured in replicates of 10 over 3 days using 2 lots of reagent for a total of 60 measurements. The LoD was calculated to be 2.2 ng/mL.

Using data from each low-level analyte, the pooled SD and %CV were calculated. The LoQ was defined as the lowest concentration with an inter-assay precision of ≤20% CV. The LoQ was determined to be 2.4 ng/mL.

Detection limits results:

Limit of Blank	Limit of Detection	Limit of Quantitation
1.6 ng/mL	2.2 ng/mL	2.4 ng/mL

The reportable range of the assay is 3.4-155.9 ng/mL.

e. Analytical specificity:

Interference:

Three 25-OH vitamin D concentrations of pooled human serum, 20 ng/mL, 30 ng/mL, and 40 ng/mL were spiked with potentially interfering endogenous substances listed below. Each sample was tested in replicates of 12 on one ARCHITECT i2000SR analyzer using one lot of reagent. The sponsor defines significant interference as a percent difference of >10% when compared to the unspiked sample. A summary of the results are provided in the table below:

Substance	Highest concentration of substance tested that demonstrated no significant interference
Conjugated bilirubin	30 mg/dL
Unconjugated bilirubin	30 mg/dL

Substance	Highest concentration of substance tested that demonstrated no significant interference
Hemoglobin	500 mg/dL
Triglycerides	500 mg/dL
Total Protein	12 g/dL
Biotin	30 ng/mL
Cholesterol	500 mg/dL
Rheumatoid factor	800 IU/mL
Goat Anti-Rabbit Antibodies	1 µg/mL

The sponsor includes the following limitation in the labeling regarding interference from triglycerides:

"The ARCHITECT 25-OH Vitamin D assay is susceptible to interference effects from triglycerides at >500 mg/dL. A triglyceride concentration of 800 mg/dL resulted in a -13.8%, -10.2%, and -17.5% bias in results for 25-OH vitamin D concentration of approximately 20 ng/mL, 30 ng/mL, and 40 ng/mL 25-OH vitamin D, respectively."

Cross reactivity:

The sponsor performed studies to evaluate if compounds similar to 25-hydroxyvitamin D cross react with the ARCHITECT 25-OH Vitamin D 5P02 assay. Cross reactivity studies were performed by spiking potential cross-reactants into three human serum pools with 25-OH vitamin D concentrations of 20 ng/mL, 30 ng/mL, and 40 ng/mL. Each sample was tested in replicates of 12 using one ARCHITECT i2000SR analyzer and one lot of reagent. Cross-reactivity was calculated using the following equation:

$$\% \text{ Cross-Reactivity} = \frac{\text{mean value spiked} - \text{mean value unspiked}}{\text{Cross-Reactant Concentration}} \times 100$$

Results from this study are summarized in the tables below:

Vitamin D2 (Ergocalciferol)

Vitamin D2 (Ergocalciferol) Concentration Added (ng/mL)	Mean spiked sample concentration (ng/mL)	% Cross-Reactivity
100.0	20.2	0.4%
100.0	29.7	0.3%
100.0	40.7	0.3%

Vitamin D3 (Cholecalciferol)

Vitamin D3 (Cholecalciferol)Concentration Added (ng/mL)	Mean spiked sample concentration (ng/mL)	% Cross-Reactivity
100.0	20.3	0.5%
100.0	30.1	0.8%
100.0	40.8	0.3%

C-3-Epimer of 25-OHD3

C-3-Epimer of 25-OHD3 Concentration Added (ng/mL)	Mean spiked sample concentration (ng/mL)	% Cross-Reactivity
100.0	20.4	0.5%
100.0	30.3	0.8%
100.0	40.4	1.3%

C-3-Epimer of 25-OHD2

C-3-Epimer of 25-OHD2 Concentration Added (ng/mL)	Mean spiked sample concentration (ng/mL)	% Cross-Reactivity
100.0	20.5	0.5%
100.0	30.2	0.6%
100.0	40.9	0.8%

1,25 $(OH)_2$ Vitamin D_3

1,25 $(OH)_2$ Vitamin D_3 Concentration Added (ng/mL)	Mean spiked sample concentration (ng/mL)	% Cross-Reactivity
100.0	20.6	0.0%
100.0	29.8	0.1%
100.0	41.3	-0.1%

1,25 $(OH)_2$ Vitamin D_2

1,25 $(OH)_2$ Vitamin D_2 Concentration Added (ng/mL)	Mean spiked sample concentration (ng/mL)	% Cross-Reactivity
100.0	20.6	-0.1%
100.0	30.6	-0.3%
100.0	41.1	-0.4%

Paracalcitrol (Zemplar)

Paracalcitrol (Zemplar) Concentration Added (ng/mL)	Mean spiked sample concentration (ng/mL)	% Cross-Reactivity
24.0	20.6	-0.3%
24.0	30.2	0.6%
24.0	41.5	0.4%

24, 25 $(OH)_2$ Vitamin D_3

24, 25 $(OH)_2$ Vitamin D_3 Concentration Added (ng/mL)	Mean spiked sample concentration (ng/mL)	% Cross-Reactivity
20.0	20.7	131.8%
20.0	30.7	101.9%
20.0	41.1	189.2%

24, 25 $(OH)_2$ Vitamin D_2

24, 25 $(OH)_2$ Vitamin D_2 Concentration Added (ng/mL)	Mean spiked sample concentration (ng/mL)	% Cross-Reactivity
20.0	20.6	102.9%
20.0	30.1	71.4%
20.0	41.0	114.2%

Cross reactivity of 25-OH Vitamin D3

The cross reactivity of 25-OH vitamin D3 was evaluated in a separate cross-reactivity study in which vitamin D depleted serum samples were spiked with known concentrations of 25-OH vitamin D3 using NIST SRM 2972 stock solution. The samples were run in replicates of 14. The cross-reactivity was calculated using the following equation:

$$\% \text{ Cross-reactivity} = \frac{\text{spiked sample mean concentration}}{\text{stock concentration added}} \times 100$$

The following cross-reactivity results were obtained for 25-OH vitamin D3:

25-OH Vitamin D3

25-OH vit D3 spiked into vitamin D depleted serum (ng/dL)	Mean spiked sample concentration (ng/dL)	% Cross-Reactivity
20.0	19.7	98.6%
30.0	30.3	101.1%
40.0	39.9	99.8%

Cross Reactivity of 25-OH Vitamin D2

The cross-reactivity of the ARCHITECT 25-OH Vitamin D 5P02 assay with 25-OH vitamin D2 was assessed using endogenous (non-spiked) serum specimens with total 25-OH vitamin D2 concentrations of approximately 26 ng/mL and 68 ng/mL and 25-OH vitamin D3 concentrations below the detection limit of the LC-MS/MS on which they concentrations were quantified. Each concentration was tested in a minimum of 2 replicates using 1 lot each of reagent, calibrators, and controls on 1 ARCHITECT i2000SR instrument. The cross-reactivity was calculated using the following equation:

$$\% \text{ Cross-reactivity} = \frac{\text{Total 25-OH vitamin D (ARCHITECT)}}{\text{25-OH vitamin D2 (LC-MS/MS)}} \times 100$$

The following cross-reactivity results were obtained for 25-OH vitamin D2

LC-MS/MS		ARCHITECT 25-OH Vitamin D	
25-OH Vit. D2 (ng/mL)	25-OH Vit. D3 (ng/mL)	Total 25-OH Vitamin D (ng/dL)	25OHD2 % Cross-Reactivity
25.6	<LoQ	20.6	80.5%
68.0	<LoQ	56.0	82.4%

f. Assay cut-off:

Not applicable

2. Comparison studies:

a. Method comparison with predicate device:

A method comparison study was performed to compare the candidate device (standardized ARCHITECT 25-OH Vitamin D 5P02 assay) to the predicate device (non-standardized ARCHITECT Vitamin D assay, k110619). A total of 107 native

serum samples were tested in duplicate using the candidate device and the predicate device. The sample concentrations ranged from 9.6-96.9 ng/mL. One ARCHITECT i2000SR analyzer and one reagent lot were used. Passing-Bablok regression analysis was performed as shown below:

ARCHITECT Vitamin D Standardized vs Unstandardized	Value
Number	107
Slope	0.99
Intercept	-1.05
R	0.98
Test range	9.6-96.9 ng/mL

An additional method comparison study was conducted to evaluate the accuracy between the candidate device and the RMP, University of Ghent's ID-LC/MS/MS method. The method comparison against the RMP was the basis of the substantial equivalence determination.

A total of 129 unaltered serum samples value assigned by ID-LC-MS/MS RMP (Ghent University), were tested in singleton on two ARCHITECT i2000SR analyzers using two lots of reagents. 120 samples were native samples, 7 samples were spiked and 3 samples were diluted in order to span the measuring range, but one spiked sample was eliminated from data analysis because the result was greater than 160 ng/mL. The test range as measured by the RMP method was 4.0 to 153.2 ng/mL. Passing-Bablok analysis was performed and the results for the first replicate of the ARCHITECT 25-OH Vitamin D assay when compared to the reference method were shown below:

ARCHITECT 25-OH Vitamin D 5P02 vs ID-LC-MS/MS RMP	Value (95% CI)
Slope	1.02 (0.99, 1.05)
Intercept	-0.99 (-1.92, -0.24)
Correlation Coefficient	0.99 (0.99,0.99)
Candidate Result Ranges	4.9 to 151.3 ng/mL

b. Matrix comparison:

A tube type comparison study was performed based on guidance from CLSI EP7-A2. Forty donor sample sets in the control tube type (serum, plastic) and in the following tube types: dipotassium EDTA, lithium heparin, sodium heparin, lithium heparin plasma separator, serum separator, and tri-potassium EDTA were collected. No more than 20% of the donor sets were supplemented with 25-OH vitamin D stock solution to create samples that spanned the measuring range of the assay. The total number of sample sets tested was 51. The control tube sample (serum) was tested in replicates of 3 for each sample and each of the other sample types were tested in a minimum of 2

replicates with the ARCHITECT 25-OH Vitamin D 5P02 assay using 2 ARCHITECT i2000SR analyzers and one lot of reagent. For each donor set, the mean concentration was calculated for the control tube type. The control tube test concentration range was 7.2 – 135.8 ng/dL. The first replicate result of each of the alternate tube types was used in the Passing-Bablok analysis which yielded the following linear regression equations:

Dipotassium (K2) EDTA: y= 0.93x + 0.76, r=1.00

Lithium heparin: y= 0.94x -0.90, r=1.00

Sodium heparin: y= 0.94x + 0.84, r=1.00

Lithium heparin plasma separator: y=0.93x – 1.09, r=1.00

Serum separator: y= 0.99x+ 0.4, r=1.00

Tri-potassium (K3) EDTA: y=0.92x + 0.83, r=1.00

Sponsor claimed that all the tube types tested above are acceptable tube type for use with the ARCHITECT 25-OH vitamin D assay.

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):

   Not applicable

4. Clinical cut-off:

   Not applicable

5. Expected values/Reference range:

   The reference range study was conducted with reference to the CLSI C28-A3 guideline. A total of 283 unaltered serum specimens from 141 females and 142 males, ages 21 to 69 years, were assayed in singleton utilizing the ARCHITECT 25-OH Vitamin D 5P02 assay on the i2000SR analyzer using 2 lots of reagents. The specimens were obtained

from the northern, central and southern regions of the United States in the Spring/Summer (April to October) and Fall/Winter (November to March). No more than 50% of the subjects were taking vitamin D supplements. None of the subjects were taking vitamin D supplements of more than 2000 IU vitamin D. Specimens with abnormal PTH, TSH, and Calcium levels were excluded from the data. The 95% reference interval was calculated by a non-parametric method and the following range was obtained:

Normal Adults: 6.2-53.2 ng/mL (n=283)

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.