

**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION  
DECISION MEMORANDUM**

**A. 510(k) Number:**

K143534

**B. Purpose for Submission:**

New device

**C. Measurand:**

Cancer Antigen 125 (CA 125)

**D. Type of Test:**

Quantitative electrochemiluminescent immunoassay

**E. Applicant:**

Roche Diagnostics

**F. Proprietary and Established Names:**

Elecsys CA 125 II Assay  
Elecsys CA 125 II CalCheck

**G. Regulatory Information:**

1. Regulation section:

21 CFR §866.6010: Tumor-associated antigen immunological test system  
21 CFR §862.1660: Quality control material (assayed and unassayed)

2. Classification:

Class II (Elecsys CA 125 II Assay)  
Class I (Elecsys CA 125 II CalCheck)

3. Product code:

LTK: Test, epithelial ovarian tumor-associated antigen (CA 125)  
JJX: Single (specified) analyte controls (Assayed and Unassayed)

4. Panel:

Immunology (82)  
Chemistry (75)

**H. Intended Use:**

1. Intended use(s):

Elecsys CA 125 II assay:

Elecsys CA 125 II is an immunoassay for the in vitro quantitative determination of OC 125 reactive determinants in human serum, Li-heparin, K2-EDTA and K3-EDTA plasma, as well as Li-heparin plasma tubes containing separating gel on the cobas e 411 analyzer.

These determinants are associated with a high molecular weight glycoprotein in serum and plasma of women with primary epithelial invasive ovarian cancer (excluding those with cancer of low malignant potential).

This immunoassay is indicated for use as an aid in the detection of residual or recurrent ovarian carcinoma. This immunoassay is further indicated for use in monitoring patients for disease progress or response to therapy.

The electrochemiluminescence immunoassay "ECLIA" is intended for use on the cobas e 411 immunoassay analyzers.

Elecsys CA 125 II CalCheck:

For use in the verification of the calibration established by the Elecsys CA 125 II reagent on the Elecsys and cobas e immunoassay analyzers.

2. Indication(s) for use:

Same as Intended Use

3. Special conditions for use statement(s):

For prescription use only

4. Special instrument requirements:

For use on the cobas e 411 analyzer

**I. Device Description:**

The Elecsys CA 125 II Assay is a kit intended for use in the measurement of OC 125 reactive determinants in human serum or plasma. The assay employs a sandwich immunoassay

format using biotinylated M11 monoclonal antibody as a capture reagent and ruthenium-labeled OC125 monoclonal antibody as a detection reagent. Streptavidin-coated microparticles are used for capture of antibody-antigen complexes and detection is by electrochemiluminescence.

Elecsys CA 125 II CalCheck calibration verification solutions comprise three levels—low, mid and high—each with a defined CA 125 concentration. The low solution concentration is near the lower detection limit of the assay. The mid solution is in the middle or at a clinically critical point of the measuring range. The high solution is near the upper limit of the measuring range.

**J. Substantial Equivalence Information:**

1. Predicate device name(s) and numbers:

Elecsys CA 125 II (k972162)  
 Elecsys CA 125 II CalCheck (k102086)

2. Comparison with predicate:

Similarities for Elecsys CA 125 II Assay		
Item	Device Elecsys CA 125 II Assay	Predicate Elecsys CA 125 II
Intended Use/ Indications for Use	<p>The Elecsys CA 125 II assay is an immunoassay for the in vitro quantitative determination of OC 125 reactive determinants in human serum, Li-heparin, K<sub>2</sub>-EDTA and K<sub>3</sub>-EDTA plasma, as well as Li-heparin plasma tubes on the cobas e 411 immunoassay analyzer.</p> <p>These determinants are associated with a high molecular weight glycoprotein in serum and plasma of women with primary epithelial invasive ovarian cancer (excluding those with cancer of low malignant potential).</p> <p>The Elecsys CA 125 II assay is indicated for use as an aid in the detection of residual or recurrent ovarian carcinoma. The Elecsys CA 125 II assay is further indicated for use in monitoring patients for disease progress or response to therapy.</p> <p>The electrochemiluminescence</p>	Same

<b>Similarities for Elecsys CA 125 II Assay</b>		
<b>Item</b>	<b>Device Elecsys CA 125 II Assay</b>	<b>Predicate Elecsys CA 125 II</b>
	immunoassay “ECLIA” is intended for use on the cobas e 411 immunoassay analyzers.	
Test Principle	Electrochemiluminescent Immunoassay	Same
Measurement Type	Quantitative	Same
Controls	Elecsys PreciControl Tumor Marker (k972235)	Same
Traceability	The method has been standardized against the Enzymun-Test CA 125 II method. This in turn has been standardized against the CA 125 II RIA from Fujirebio Diagnostics.	Same
Reagent Stability	Unopened at 2–8 °C: up to the stated expiration date After opening at 2–8 °C: 12 weeks	Same
Calibration Interval	After 7 days (when using the same reagent kit on the analyzer) As required, e.g. quality control findings outside the defined limits.	Same

<b>Differences for Elecsys CA 125 II Assay</b>		
<b>Item</b>	<b>Device Elecsys CA 125 II Assay</b>	<b>Predicate Elecsys CA 125 II</b>
Instrument(s)	cobas e 411	Elecsys 2010, cobas e 411, MODULAR <i>Analytics</i> E170, cobas e 601, cobas e 602
Sample Types	Serum collected using standard sampling tubes or tubes containing separating gel. Li-heparin, K <sub>2</sub> -EDTA and K <sub>3</sub> -EDTA, as well as Li-heparin plasma tubes containing separating gel.	Serum collected using standard sampling tubes or tubes containing separating gel. Plasma treated with Na-heparin, K <sub>3</sub> -EDTA, or sodium citrate
Measuring Range	2.0–3000 U/mL	0.6–5000 U/mL
Sensitivity	LoB = 0.6 U/mL LoD = 1.2 U/mL LoQ = 2.0 U/mL	Lower Detection Limit = 0.6 U/mL
Sample:Reagent Ratio	20:70 uL	40:60 uL
Calibrator	Elecsys CA 125 II CalSet II (k140112)	Elecsys CA 125 II CalSet (k003969)

<b>Differences for Elecsys CA 125 II Assay</b>		
<b>Item</b>	<b>Device Elecsys CA 125 II Assay</b>	<b>Predicate Elecsys CA 125 II</b>
Reagent Stability	On the analyzers: 6 weeks	On the analyzers: 4 weeks
Calibration Interval	After 8 weeks when using the same reagent lot	After 1 month (28 days) when using the same reagent lot

<b>Similarities for Elecsys CA 125 CalCheck</b>		
<b>Item</b>	<b>Device Elecsys CA 125 II CalCheck</b>	<b>Predicate Elecsys CA 125 II CalCheck 5</b>
Analyte	CA 125	Same
Format	Lyophilized	Same
Stability	Unopened at 2–8 °C: up to the stated expiration date After opening at 20–25 °C: 4 hours	Same
Instruments	Elecsys and cobas e immunoassay analyzers	Same

<b>Differences for Elecsys CA 125 CalCheck</b>		
<b>Item</b>	<b>Device Elecsys CA 125 II CalCheck</b>	<b>Predicate Elecsys CA 125 II CalCheck</b>
Intended Use/Indication for Use	For use in the verification of the calibration established by the Elecsys CA 125 II reagent on the indicated Elecsys and cobas e immunoassay analyzers.	The Elecsys CA 125 II CalCheck 5 is an assayed control for use in calibration verification and for use in the verification of the assay range established by the Elecsys CA 125 II reagent on the indicated Elecsys and cobas e immunoassay analyzers
Levels	Three	Five
Handling	Reconstitute Check 1, Check 2, and Check 3 with exactly 1.0mL distilled or deionized water. Allow to stand closed for 15 minutes, then mix gently by inversion.	Reconstitute Check 1, Check 2, Check 3, Check 4 and Check 5 with exactly 1.0mL distilled or deionized water. Allow to stand closed for 15 minutes, then mix gently by inversion.
Matrix	Level 1: Equine serum	Level 1: Equine serum

Differences for Elecsys CA 125 CalCheck		
Item	Device Elecsys CA 125 II CalCheck	Predicate Elecsys CA 125 II CalCheck
	Levels 2 & 3: Human serum matrix	Levels 2–5: Human serum matrix

**K. Standard/Guidance Documents Referenced:**

CLSI EP05–A3: Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline

CLSI EP06–A: Evaluation of the Linearity of Quantitative Analytical Methods

CLSI EP17–A2: Protocols for Determination of Limits of Detection and Limits of Quantitation, Approved Guideline

**L. Test Principle:**

The Elecsys CA 125 II assay is a two-step sandwich immunoassay. First, sample is incubated with a biotinylated monoclonal CA 125-specific antibody and a monoclonal CA 125-specific antibody labeled with a ruthenium to form a sandwich complex. After addition of streptavidin-coated microparticles, the complex binds to the solid phase via interaction of biotin and streptavidin. The reaction mixture is aspirated into the measuring cell where the microparticles are magnetically captured onto the surface of the electrode. Unbound substances are then removed. A voltage is applied to the electrode to induce chemiluminescent emission which is measured by a photomultiplier. The results are determined via a calibration curve that is instrument-specifically generated by 2-point calibration and a master curve provided via the reagent barcode.

**M. Performance Characteristics:**

1. Analytical performance:

*a. Precision/Reproducibility:*

Total Imprecision: Six human sera were measured with two replicates and two runs per day for 20 days (n = 80). The human sera were pooled patient and single donor spiked samples. Samples were measured using one lot of reagent, on one instrument (cobas e 411), at two different sites as indicated in the table below. Analysis of variance (ANOVA) was used to calculate repeatability and reproducibility according to CLSI EP05-A3. All data met the manufacturer’s acceptance criteria for % CV and 95% confidence intervals for % CV.

Sample	Mean (U/mL)	Within-Run		Between-Run		Between-Day		Total	
		SD	CV	SD	CV	SD	CV	SD	CV
1	3.1	0.09	2.8%	0.05	1.5%	0.08	2.7%	0.13	4.2%
2	14.7	0.43	2.9%	0.15	1.0%	0.38	2.6%	0.59	4.0%
3	35.0	0.69	2.0%	0.27	0.8%	0.72	2.1%	1.04	3.0%
4	2399	59.5	2.5%	8.24	0.3%	52.3	2.2%	79.6	3.3%
5*	121	1.13	0.9%	0.79	0.7%	0.63	0.5%	1.52	1.3%
6*	330	3.61	1.1%	1.88	0.6%	1.80	0.5%	4.45	1.3%

\*Samples were tested at a site that is different from the first four samples

**Site-to-Site Reproducibility:** Five human sera were measured with two replicates and two runs per day for 10 days (n= 40), using one lot of reagent and one instrument (cobas e 411) at three different sites. The human sera were pooled patient and single donor spiked samples. At Site 1, the total precision for the five samples ranged from 1.4%–1.7% CV. At Site 2, the total precision for the five samples ranged from 0.9%–1.5% CV. At Site 3, the total precision for the five samples ranged from 2.4%–3.0% CV. The combined site-to-site reproducibility parameters are detailed in the table below. All values met the manufacturer’s acceptance criteria.

Sample	Mean (U/mL)	Within-Run		Between-Run		Between-Day		Between-Sites		Total	
		SD	CV	SD	CV	SD	CV	SD	CV	SD	CV
1	15.3	0.17	1.1%	0.13	0.8%	0.24	1.6%	0.40	2.6%	0.52	3.4%
2	48.6	0.49	1.0%	0.36	0.7%	0.64	1.3%	1.29	2.6%	1.56	3.2%
3	49.2	0.39	0.8%	0.39	0.8%	0.75	1.5%	1.39	2.8%	1.68	3.4%
4	122	1.04	0.9%	0.89	0.7%	1.57	1.3%	2.45	2.0%	3.22	2.6%
5	331	3.14	1.0%	2.01	0.6%	4.41	1.3%	6.34	1.9%	8.57	2.6%

**Lot-to-Lot Reproducibility:** Four human sera were measured with two replicates and two runs per day for 10 days (n= 40) using three lots of reagents on one instrument (cobas e 411) at one site. The human sera were pooled patient and single donor spiked samples. For Lot 1, the total precision for the four samples ranged from 3.4%–8.3% CV. For Lot 2, the total precision for the four samples ranged from 5.2%–8.6% CV. For Lot3, the total precision for the four samples ranged from 3.3%–4.7%. The combined lot-to-lot reproducibility parameters are detailed in the table below. All values met the manufacturer’s acceptance criteria.

Sample	Mean	Within-Run		Between-Run		Between-Day		Between-Lots		Total	
		SD	CV	SD	CV	SD	CV	SD	CV	SD	CV
1	3.06	0.13	4.1%	0.01	0.4%	0.18	6.0%	0.08	2.7%	0.24	7.8%
2	14.98	0.39	2.6%	0.00	0.0%	0.51	3.4%	0.44	2.9%	0.77	5.2%
3	35.4	1.00	2.8%	0.00	0.0%	1.44	4.1%	0.63	1.8%	1.87	5.3%
4	2418	71.0	2.9%	0.00	0.0%	88.7	3.7%	34.0	1.4%	118	4.9%

*b. Linearity/assay reportable range:*

Linearity: The studies followed CLSI EP06-A, where 15 dilutions were prepared by diluting three human serum samples and three human plasma samples spiked with CA 125 down across the lower end of the measuring range. Each dilution was measured in three replicates on cobas e411. Results are summarized in the following table:

Sample	Dilution range (U/mL)	Slope (95% CI)	Intercept (95% CI)	R <sup>2</sup>	%CV Range
Serum Sample 1	0.31–3290	0.95 (0.95–0.95)	0.02 (-0.224–0.271)	0.99	-0.2%–0.9%
Serum Sample 2	0.32–3139	1.00 (1.00–1.01)	0.14 (-0.14–0.42)	0.99	-1.1%–6.7%
Serum Sample 3	0.31–3271	0.89 (0.88–0.89)	0.10 (-0.15–0.35)	0.99	-1.6%–3.0%
Plasma Sample 1	0.30–3197	0.89 (0.88–0.90)	0.00 (-0.39–0.40)	0.99	-3.8%–3.8%
Plasma Sample 2	0.27–3210	0.88 (0.88–0.89)	0.30 (-0.10–0.70)	0.99	-3.5%–1.7%
Plasma Sample 3	0.40–3241	0.88 (0.87–0.89)	0.03 (-0.36–0.43)	0.99	-5.4%–2.7%

The data support linearity from 2.0–3000 U/mL. Values below the LoD are reported as <2.0 U/mL and values above the measuring range as >3000 U/mL.

Automatic dilution versus manual dilution: Three human serum samples were spiked with CA 125 to concentrations above the analytical measuring range. These samples were diluted 1:5 manually or automatically on the cobas e 411 analyzer using Diluent Universal. Each sample was measured in triplicate with one lot on one analyzer and the median value was used to compare percent recovery of the manual dilution to that of the automated dilution. The manufacturer’s acceptance criteria of percent recovery 90–110% were met.

High dose hook effect: Hook effect was measured using two human serum samples spiked with CA 125 to 50000 U/mL. Each sample was then diluted with Diluent

Universal to a level below the upper limit of the analytical measuring range and measured with a single replicate using one lot of reagent and one analyzer (cobas e 411). The data demonstrated the assay is not susceptible to antigen excess up to a concentration of 50000 U/mL.

*c. Traceability and Stability:*

*i. Traceability:*

There are no reference standards for CA 125. The results are reported in U/mL and the method has been standardized against the Enzymun-Test CA 125 II method. This in turn has been standardized against the CA 125 II RIA from Fujirebio Diagnostics.

*ii. Kit Stability:*

Shelf-Life Stability: A real-time stability study set the shelf-life stability of the Elecsys CA 125 II assay at 18 months when stored at 2–8°C.

Open-Vial Stability: The assay reagents can be stored opened at 2–8°C for up to 12 weeks.

On-Board Stability: The assay reagents can be stored on-board the cobas e 411 analyzer at 20±3°C for up to 6 weeks.

*iii. Sample Stability:*

Ten human samples for each sample type (serum, K<sub>2</sub>-EDTA-plasma, K<sub>3</sub>-EDTA-plasma, Li-heparin-plasma) that covered the analytical measuring range were tested under four different conditions: 2–8°C, 15–25°C, -20°C, and after multiple freeze/thaw cycles. Each sample was measured with three replicates and percent recovery was compared to the sample stored at -80°C. Samples were determined to be stable for up to 5 days at 2–8°C, up to 8 hours at 15–25°C, up to 24 weeks at -20°C or following 2 freeze/thaw cycles.

*d. Detection limit:*

The Limit of Blank (LoB) and Limit of Detection (LoD) were determined according to CLSI EP17-A2. To estimate LoB, five measurand-free human serum samples were measured in six runs on two instruments with three different reagent lots (n = 60 replicates per reagent lot). LoB was calculated as the highest 95<sup>th</sup> percentile value from the three reagent lots. The LoB was determined to be 0.6 U/mL. To determine LoD, five human serum samples with low analyte values were measured in six runs on two instruments with three different reagent lots (n = 60 replicates per reagent lot). LoD was calculated from the following equation:  $LoD = LoB + 1.653 \times (\text{total standard deviation})$ . The Limit of Quantitation (LoQ) was determined using six

pooled human serum samples that were diluted to have CA 125 concentrations between 1.0-6.3 U/mL. Each sample was measured in six runs, on two instruments, with three different reagent lots (n = 72 replicates per reagent lot). The detection limit values are presented in the table below:

<b>LoB</b>	<b>LoD</b>	<b>LoQ</b>
0.6 U/mL	1.2 U/mL	2.0 U/mL

e. *Analytical specificity:*

i. *Endogenous Interference:*

Interferences were assessed by testing two human serum samples with CA 125 concentrations of 35 and 2260 U/mL. Each sample was split in half, and a high concentration of each potentially interfering endogenous substance was spiked into one half. The spiked sample was then mixed with the non-spiked half to create a series of eleven samples containing different concentrations of the potential interferent and tested in a single replicate. The manufacturer's acceptance criteria for non-interference were met and the assay was not affected by the following substances at the indicated concentrations:

<b>Interfering Substance</b>	<b>Final Test Concentration</b>
Biotin	70 ng/mL
Triglycerides (Intralipid)	3800 mg/dL
Bilirubin	75 mg/dL
Rheumatic Factor	1500 IU/mL
Hemoglobin	3200 mg/dL
HAMA	805 µg/mL

ii. *Exogenous Interference:*

A total of 16 common drugs and 23 cancer drugs were tested for interference using two spiked human serum samples with CA 125 concentrations of 11 and 313 U/mL. Each sample was spiked with a high concentration of interferent and measured with three replicates in one run using one reagent lot on one analyzer (cobas e 411). The manufacturer's acceptance criteria for non-interference were met and the assay was not affected by the following drugs at the indicated concentrations:

Final Test Concentration (mg/L)			
Common Drugs		Cancer Drugs	
Acetylcysteine	553	Carboplatin	1000
Ampicillin-Na	1000	Cisplatin	225
Ascorbic Acid	300	Cyclophosphamide	1000
Cyclosporine	5	Dexamethasone	20
Cefoxitin	2500	Docetaxel (Taxotere)	112
Heparin	5000 U	Doxorubicin	75
Levodopa	20	Pegylated, Liposomal Doxorubicin (CAELYX)	75
Methyldopa +1.5	15	Leucovorin	750
Metronidazole	200	Melphalan	15
Phenylbutazone	400	Methotrexate	1000
Doxycycline	30	Lynparza (Olaparib)	800
Acetylsalicylic Acid	1000	Paclitaxel	265
Rifampicin	64	5-Fluorouracil	500
Acetaminophen	200	Avastin	750
Ibuprofen	500	Tarceva	150
Theophylline	100	MabThera	750
		Herceptin	600
		Tamoxifen	50
		Mitomycin	25
		Etoposide	400
		Flutamide	1000
		Gemcitabine	1500
		Taxol	5.5

*f. Assay Cut-Off:*

Not applicable

2. Comparison studies:

*a. Method comparison with predicate device:*

A total of 80 native, single-donor human serum samples spanning the dynamic range (4.7–2680 U/mL) were assayed in singleton with the predicate device and the new device on the Elecsys 2010 analyzer using CA 125 II Cal Set (k003969). Regression statistics are based on the balance of the paired results and the data are as follows:

Regression Fit	Regression Equation	Slope (95% CI)	Intercept (95% CI)	R <sup>2</sup>
Passing-Bablok	$y = 0.98x + 1.2$	0.94 to 1.00	0.33–1.82	0.99

b. *Comparison between previous and updated calibrators:*

A total of 111 native, single donor human serum samples spanning the dynamic range (3.2–2,621 U/mL) were assayed in singleton with the new device on the cobas e 411 analyzer using either the previous calibrator set (Elecsys CA 125 II Cal Set, K003969) or the updated calibrator set (Elecsys CA 125 II Cal Set II, K140112). Regression statistics are based on the balance of the paired results and the data are as follows:

Regression Fit	Regression Equation	Slope (95% CI)	Intercept (95% CI)	R <sup>2</sup>
Passing-Bablok	$y = 0.99x - 0.82$	0.993–0.994	-0.827–-0.818	1.00

c. *Matrix comparison*

A study was performed to demonstrate that heparin plasma (Li-heparin or drawn into Li-heparin Plasma Separation Tubes) and EDTA (K<sub>2</sub>-EDTA-, K<sub>3</sub>-EDTA) plasma matrices yield comparable values as serum in the Elecsys CA 125 II assay. A total of 51 or 52 matrix-matched samples spread across the assay range (2.2–2980 U/mL) were assayed in duplicate using one reagent lot and one analyzer (cobas e 411). Passing-Bablok regression analysis was performed and the corresponding slopes of regression and coefficient determination are summarized in the following table:

Plasma Type	N	Range Tested (U/mL)	Slope (95% CI)	Intercept (95% CI)	Correlation
Li-Heparin	52	2.3–2980	0.98 (0.94–0.99)	0.11 (-0.03–0.48)	1.0
K <sub>2</sub> -EDTA	51	2.3–2962	0.98 (0.97–0.99)	0.04 (-0.26–0.13)	1.0
K <sub>3</sub> -EDTA	51	2.3–2962	1.00 (0.96–1.02)	-0.45 (-0.74–-0.01)	1.0
Li-Heparin Separation Tubes	51	2.3–2980	0.98 (0.92–1.00)	-0.35 (-0.69–0.18)	1.0

3. Clinical studies:

Not Applicable

4. Clinical cut-off:

Not Applicable

5. Expected values/Reference range:

Expected Values in Normal Healthy Individuals: To determine the reference range of the Elecsys CA 125 II assay in healthy women, 120 pre-menopausal and 120 post-menopausal women were tested (total = 240 subjects). Ages ranged from 18 to 87 years and represented whites (96%), Hispanic/Latino (0.4%), Asian (0.4%) and African American (2.5%) subjects. The mean, SD, median, range and 5<sup>th</sup> to 95<sup>th</sup> percentile of CA125 concentrations, and percent below the upper limit of normal (ULN) as observed in the data, are shown for each group in the table below.

<b>Healthy Subjects</b>	
Premenopausal	120
Postmenopausal	120
Total Samples	240
Age Range (years)	18–87
<b>Results (U/mL)</b>	
Mean	17.2
Standard Deviation	11.9
Median	14.1
Min	4.1
Max	127
5 <sup>th</sup> Percentile	6.4
95 <sup>th</sup> Percentile	38.1
Percent below ULN*	95%

Expected Values in Non-Ovarian Malignancy Conditions: To evaluate the performance of the Elecsys CA 125 II assay in subjects with other malignant and benign conditions, the assay was evaluated in 199 subjects with various cancers (bladder cancer, breast cancer, gastrointestinal cancer, endometrial cancer, lung cancer) and in 411 women with benign conditions. A total of 80 women with conditions other than cancers (hypertension and pregnancy) were also included. A total of 690 specimens were analyzed. The mean, standard deviation, mean, 5<sup>th</sup> to 95<sup>th</sup> percentiles of CA125 concentrations, and percent below the ULN, as observed in the data, are shown for each condition group. Elevated CA 125 concentrations can be found in samples from patients with serositis or other

tumors besides ovarian carcinoma, endometrial carcinoma and carcinoma of the fallopian tube.

<b>Subjects with Non-Ovarian Malignancies</b>					
	<b>Endometrial</b>	<b>Breast</b>	<b>Gastro-intestinal</b>	<b>Lung</b>	<b>Bladder</b>
Premenopausal	12	12	9	3	2
Postmenopausal	28	28	31	37	37
Total Samples	40	40	40	40	39
Age Range (years)	35–83	39–92	33–85	43–82	30–91
<b>Results U/mL</b>					
Mean	87.2	70.6	34.2	32.7	29.2
Standard Deviation	202	144	57.8	18.7	36.5
Median	20.6	18.5	16.2	30.2	18.5
Min	6.9	4.5	7.1	9.3	4.4
Max	1117	811	306	64.3	215
5 <sup>th</sup> Percentile	8.6	4.8	7.2	10.6	5.8
95 <sup>th</sup> Percentile	656	348	231	62.3	101
Percent below ULN*	70%	75%	82%	58%	82%

<b>Subjects with Benign Conditions and Conditions Other than Cancers</b>				
	<b>Benign Gynecologic</b>	<b>Benign Non-Gynecologic</b>	<b>Pregnant</b>	<b>Hypertension</b>
Premenopausal	219	2	40	4
Postmenopausal	152	38	0	36
Total Samples	371	40	40	40
Age Range (years)	18–89	25–89	19–40	36–91
<b>Results (U/mL)</b>				
Mean	44.4	38.6	20.6	20.8
Standard Deviation	94.0	87.4	10.0	16.6
Median	20.6	15.8	18.0	15.9
Min	4.2	3.6	11.5	6.0
Max	995	541	64.9	89.1
5 <sup>th</sup> Percentile	7.8	6.4	12.0	6.2
95 <sup>th</sup> Percentile	132	183	44.9	61.8
Percent below ULN*	76%	85%	92%	90%

\*ULN is calculated as the 95<sup>th</sup> percentile value for apparently health women. For this assay, the ULN = 38.1 U/mL.

**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.