DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
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Silver Spring, MD 20993-0002

August 6, 2015

Roche Professional Diagnostics
Linda McCammack
Regulatory Program Manager
9115 Hague Road
Indianapolis, IN 46250

Re: K143534
Trade/Device Name: Elecsys CA 125 II Assay
Elecsys CA 125 II CalCheck
Regulation Number: 21 CFR 866.6010
Regulation Name: Tumor-associated antigen immunological test system
Regulatory Class: II
Product Code: LTK, JJX
Dated: July 6, 2015
Received: July 7, 2015

Dear Ms. McCammack:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the

electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulations (21 CFR Parts 801 and 809), please contact the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely yours,

Leonthena R. Carrington -S

Leonthena R. Carrington, MS, MBA, MT(ASCP)
Director
Division of Immunology and Hematology Devices
Office of In Vitro Diagnostics and Radiological Health
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: January 31, 2017
See PRA Statement below.

510(k) Number *(if known)*
K143534

Device Name
Elecsys CA 125 II Assay

Indications for Use *(Describe)*
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, 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.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

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DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: January 31, 2017
See PRA Statement below.

510(k) Number *(if known)*
K143534

Device Name
Elecsys CA 125 II CalCheck

Indications for Use *(Describe)*
For use in the verification of the calibration established by the Elecsys CA 125 II reagent on the Elecsys and cobas e immunoassay analyzers.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

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510(k) Summary for the Elecsys CA 125 II assay and Elecsys CA 125 II CalCheck

Introduction

According to the requirements of 21 CFR 807.92, the following information provides sufficient detail to understand the basis for a determination of substantial equivalence.

Submitter Name, Address, Contact

Roche Diagnostics
9115 Hague Road
P.O. Box 50416
Indianapolis, IN 46250-0415

Contact Person: Linda McCammack

- Phone: (317) 521-7144
- Fax: (317) 521-2324
- Email: linda.mccammack@roche.com

Secondary Contact Person: Angelo Pereira

- Phone: (317) 521-3544
- Fax: (317) 521-2324
- Email: angelo.pereira@roche.com

Date Updated: August 6, 2015

Purpose

In accordance with 21 CFR 807.87, Roche Diagnostics hereby submits official notification as required by Section 510(k) of the Federal Food, Drug and Cosmetics Act of our intention to market the device described in this Premarket Notification 510(k).

The purpose of this premarket notification is to modernize the label for the Elecsys CA 125 II assay, which currently does not contain information on LoB, LoD or LoQ. In addition, we would like to include new data for precision on the **cobas e** instruments in our product labeling.

Information is also provided on a new Elecsys CA 125 II CalCheck product.

Continued on next page

510(k) Summary for Elecsys CA 125 II assay, *continued*

Device Name	Proprietary name:	Elecsys CA 125 II Assay
	Common name:	CA 125 II assay
	Classification name:	Test, Epithelial Ovarian Tumor Associated Antigen (Ca125)
	Product Code:	LTK
	Predicate Device:	Elecsys CA 125 II (k972162)
Device Name	Proprietary name:	Elecsys CA 125 II CalCheck
	Common name:	CA 125 II CalCheck
	Classification name:	Single (specified) analyte controls (assayed and unassayed)
	Product Code:	JJX
	Predicate Device:	Elecsys CA 125 II CalCheck 5 (k102086)

Establishment Registration

For the Elecsys CA 125 II assay and the CA 125 II CalCheck, the establishment registration number for Roche Diagnostics GmbH in Mannheim, Germany, is 9610126 and for Penzberg, Germany, is 9610529. The establishment registration number for Roche Diagnostics in the United States is 1823260

Device Description

The CA 125 II assay employs a sandwich test principle using biotinylated monoclonal CA 125-specific antibody and a monoclonal CA 125-specific antibody labeled with a ruthenium complex to form a sandwich complex. The use of streptavidin-coated microparticles serves as the solid phase for the 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 (5-point-calibration) provided with the reagent bar code.

The CA 125 II application is identical to the predicate assay (k972162). This submission is being done to modernize the labeling by adding the LoB, LoD and LoQ data and to change the sample:reagent ratio from 40:60µL to 20:70µL. Additionally, based on internal stability data the calibration frequency has been extended from 4 to 8 weeks.

510(k) Summary for Elecsys CA 125 II assay, *continued*

Device Description, *continued*

The Elecsys CA 125 II CalCheck is a lyophilized product consisting of equine serum in level 1 and human serum matrix for levels 2 and 3. During manufacture, the analyte is spiked into the matrix at the desired concentration levels.

510(k) Summary for Elecsys CA 125 II assay, *continued*

Intended Use/ Indications for Use

Elecsys CA 125 II Assay:

Immunoassay for the in vitro quantitative determination of OC 125 reactive determinants in human serum, Li-heparin, K_2-EDTA and K_3-EDTA, 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 indicated Elecsys and cobas e immunoassay analyzers.

Substantial Equivalence

The Elecsys CA 125 II assay is equivalent to Elecsys CA 125 II assay (k972162).

The Elecsys CA 125 II CalCheck is equivalent to the Elecsys CA 125 II CalCheck 5 (k102086)

Substantial Equivalence - Comparison

The following table compares the Elecsys CA 125 II Assay with its predicate device (k972162).

Continued on next page

510(k) Summary for Elecsys CA 125 II, *continued*

Comparison of Assays, Similarities and Differences
Table 1

Assay Comparison		
Feature	**Predicate Device: Roche Elecsys CA 125 II (k972162)**	**Candidate Device: Elecsys CA 125 II Assay**
General Assay Features		
Intended Use/ Indications for Use	Immunoassay for the in vitro quantitative determination of OC 125 reactive determinants in human serum and plasma. 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). The Elecsys CA 125 II assay is indicated for use as an aid in the detection of residual or recurrent ovarian carcinoma in patients who have undergone first-line therapy and would be considered for second-look procedures. The Elecsys CA 125 II assay is further indicated for serial measurement of CA 125 to aid in the management of cancer patients. The electrochemiluminescence immunoassay "ECLIA" is intended for use on Elecsys and **cobas e** immunoassay analyzers.	Immunoassay for the in vitro quantitative determination of OC 125 reactive determinants in human serum, Li-heparin, K_2-EDTA and K_3-EDTA, 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 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.
Assay Protocol	The CA 125 II Assay employs a sandwich test principle using biotinylated monoclonal CA 125-specific antibody and a monoclonal CA 125-specific antibody labeled with a ruthenium complex to form a sandwich complex. The use of streptavidin-coated microparticles serves as the solid phase for the electrochemiluminescence detection.	Same.

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510(k) Summary for Elecsys CA 125 II, *continued*

Table 1, *continued*

Assay Comparison		
Feature	**Predicate Device: Elecsys CA 125 II (k972162)**	**Candidate Device: Elecsys CA 125 II Assay**
General Assay Features		
Detection Protocol	Electrochemiluminescent Assay	Same.
Applications	18 minute application	Same.
Instrument Platform	Elecsys 2010, **cobas e** 411, MODULAR *Analytics* E170, **cobas e** 601 and **cobas e** 602 immunoassay analyzers.	**cobas e** 411 analyzer
Sample: Reagent Ratio	40:60 µL	20:70 µL
Sample Type	Human serum and plasma treated with Li-, Na-. NH_4^+-heparin, K_2-EDTA, K_3-EDTA, sodium citrate plasma as well as Li-heparin plasma tubes containing separating gel. When sodium citrate is used, the results must be corrected by +10%.	Human serum and Li-heparin, K_2-EDTA and K_3-EDTA, as well as Li-heparin plasma tubes containing separating gel
Reagents	The sample is incubated with a biotinylated monoclonal CA 125-specific antibody, and a monoclonal CA 125 specific antibody labeled with a ruthenium complex to form a sandwich complex. Steptavidin-coated microparticles are added in the second incubation.	Same.
Calibrator	Elecsys CA 125 II CalSet (k003969)	Elecsys CA 125 II CalSet II (k140112)

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510(k) Summary for Elecsys CA 125 II, *continued*

Table 1, *continued*

Assay Comparison		
Feature	**Predicate Device: Elecsys CA 125 II (k972162)**	**Candidate Device: Elecsys CA 125 II Assay**
General Assay Features		
Calibration Interval	Calibration must be performed once per reagent lot using fresh reagent (i.e. not more than 24 hours since the reagent kit was registered on the analyzer). Renewed calibration is recommended as follows: • After 1 month (28 days) when using the same reagent lot. • After 7 days (when using the same reagent kit on the analyzer). • As required: e.g. quality control findings outside the specified limits	Calibration must be performed once per reagent lot using fresh reagent (i.e. not more than 24 hours since the reagent kit was registered on the analyzer). Renewed calibration is recommended as follows: • After 8 weeks when using the same reagent lot • After 7 days (when using the same reagent kit on the analyzer) • As required, e.g. quality control findings outside the defined limits.
Controls	Elecsys PreciControl Tumor Marker (k972235).	Same.
Traceability/ Standardiz-ation	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	Store at 2-8 ºC. Store the reagent kit upright in order to ensure complete availability of the microparticles during automatic mixing prior to use. Stability: Unopened at 2-8 ºC—up to the stated expiration date After opening at 2-8 ºC—12 weeks On the analyzers—4 weeks	Store at 2-8 ºC. Store the reagent kit upright in order to ensure complete availability of the microparticles during automatic mixing prior to use. Stability: Unopened at 2-8 ºC—up to the stated expiration date After opening at 2-8 ºC—12 weeks On the analyzers—6 weeks

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510(k) Summary for Elecsys CA 125 II, *continued*

Table 1, *continued*

Assay Comparison		
Feature	**Predicate Device: Elecsys CA 125 II (k972162)**	**Candidate Device: Elecsys CA 125 II Assay**
Labeled Performance Characteristics		
Measuring Range	0.6 (LDL) - 5000 U/mL	2 (LoQ) –3000 U/mL
Precision	*Elecsys 2010* Intra-Assay 3.3% CV @ 7.83 U/mL 2.1% CV @ 38.30 U/mL 2.1% CV @ 70.80 U/mL 1.9% CV @ 39.00 U/mL 1.4% CV @ 121.41 U/mL Total 4.2% CV @ 7.83 U/mL 3.1% CV @ 38.30 U/mL 2.5% CV @ 70.80 U/mL 2.5% CV @ 39.00 U/mL 2.7% CV @ 121.41 U/mL	***cobas e****411 analyzers* Within-run (Repeatability) 3.1% CV @ 14.70 U/mL 3.0% CV @ 3.07 U/mL 2.6% CV @ 2399 U/mL 1.9% CV @ 34.95 U/mL 0.9% CV @ 120.7 U/mL 1.1% CV @ 329.6 U/mL Total (Intermediate) 4.1% CV @ 14.70 U/mL 4.2% CV @ 3.07 U/mL 3.4% CV @ 2399 U/mL 3.0% CV @ 34.95 U/mL 1.3% CV @ 120.7U/mL 1.3% CV @ 329.6U/mL
LoB	Not Reported	0.6 U/mL
LoD	Not Reported	1.2 U/mL
LoQ	Not Reported	2 U/mL
Lower Detection Limit	Functional Sensitivity: 0.6 U/mL	N/A

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510(k) Summary for the Elecsys CA 125 II, *continued*

Table 1, *continued*

Assay Comparison		
Feature	**Predicate Device: Elecsys CA 125 II**	**Candidate Device: Elecsys CA 125 II Assay**
Performance Characteristics		
Hook Effect	There is no high-dose hook effect at CA 125 concentrations up to 20,000 U/mL.	There is no high-dose hook effect at CA 125 concentrations up to 50,000 U/mL.
Limitations	The assay is unaffected by: • Hemoglobin < 3.2 g/dL • Bilirubin < 75 mg/dL • Triglycerides < 3,800 mg/dL • Biotin < 50 ng/mL • Rheumatoid factors < 1,500 IU/mL • In-vitro tests were performed on 27 commonly used pharmaceuticals. No interference with the assay was found. • In rare cases, interference due to extremely high titers of antibodies to analyte-specific antibodies, streptavidin or ruthenium can occur. These effects are minimized by suitable test design. • For diagnostic purposes, the results should always be assessed in conjunction with the patient's medical history, clinical examination and other findings.	The assay is unaffected by: • Hemolysis < 3.2 g/dL • Bilirubin < 66 mg/dL • Lipemia < 2000 mg/dL • Biotin < 35 ng/mL • Rheumatoid factors < 1,200 IU/mL • In-vitro tests were performed on 16 commonly used pharmaceuticals and 23 special drugs. No interference with the assay was found. • In rare cases, interference due to extremely high titers of antibodies to analyte-specific antibodies, streptavidin or ruthenium can occur. These effects are minimized by suitable test design. • For diagnostic purposes, the results should always be assessed in conjunction with the patient's medical history, clinical examination and other findings.
Method Comparison (sample/ reagent ratio)		
	n = 80	**Passing/Bablok**
	Min = 4.7 U/mL	
	Max = 2680 U/mL	
	Slope (95% confidence limits)	0.981 (0.946 – 1.005)
	Intercept (95% confidence limits)	1.20 (0.296 – 1.77)
	Correlation (Pearson)	0.995
	Kendall (tau)	0.966

510(k) Summary for the Elecsys CA 125 II, *continued*

Table 1, *continued*

Assay Comparison		
Feature	**Predicate Device: Elecsys CA 125 II (k972162)**	**Candidate Device: Elecsys CA 125 II Assay**
Performance Characteristics		
Method Comparison **(CalSet)**		

n= 111	**Passing/ Bablok**
Min = 3.19 U/mL	Max = 2621 U/mL
Slope (95% confidence limits)	1.006 (1.006-1.006)
Intercept (95% confidence limits)	0.827 (0.824-0.829)
Correlation (Pearson)	1.000
Kendall tau	1.000

The table below compares Elecsys CA 125 II CalCheck with the predicate CA 125 II CalCheck 5

Comparison of CalCheck Products, Similarities and Differences

Table 2

Characteristic	**Predicate Device: Elecsys CA 125 II CalCheck 5 (K102086)**	**Candidate Device: Elecsys CA 125 II CalCheck**
Intended Use	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	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.
Analyte	CA 125	Same
Levels	Five	Three
Format	Lyophilized	Same
Handling	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.	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.
Stability	<u>Unopened :</u> • Store at 2-8°C until expiration date	Same

510(k) Summary for the Elecsys CA 125 II, *continued*

	Reconstituted: • 20-25°C: 4 hours	
Matrix	Level 1: Equine serum Levels 2-5: Human serum matrix	Level 1: Equine serum Levels 2 & 3: Human serum matrix

510(k) Summary for the Elecsys CA 125 II, *continued*

Evaluations Summary

The Elecsys CA 125 II reagent was evaluated for several performance characteristics, including precision, limit of blank, limit of detection, limit of quantitation, linearity, dilution, high dose hook effect, HAMA effect, interferences, method comparison, stability, and control recovery.

Precision

Precision of the Elecsys CA125 II assay was evaluated on the **cobas e** 411 immunoassay analyzer according to CLSI EP5-A2 guideline.

Precision was determined for 4 serum samples at one site using one Elecsys reagent lot and controls; 2 runs per day in duplicate each for 20 days (n=80). Precision was determined at another site for the remaining 2 serum samples using the same protocol. The measurements were performed on the **cobas e** 411 analyzer, with one reagent lot, performing rackpack calibration according to the instructions for use.

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510(k) Summary for the Elecsys CA 125 II, *continued*

Evaluations Summary, *continued*

Limit of Blank

LoB of the Elecsys CA125 II assay has been determined according to CLSI EP17-A2.

Limit of Blank is the highest observed measured value for samples free of analyte. The Limit of Blank was determined as the 95th percentile of the measurement of blank samples.

The distribution of values for five analyte-free human samples was determined with three reagent lots on two **cobas e** 411 analyzers with six runs distributed over a period of up to 5 days.

The sample was measured in one-fold determination in each run. In summary, 30 measuring points were collected per instrument. for a total of 60 measured values.

Limit of Detection

LoD of the Elecsys CA125 II assay has been determined according to CLSI EP17-A2.

LoD determines the lower limit for samples with analyte. The LoD was determined as the lowest amount of analyte in a sample that can be detected with a 95% probability.

The distribution of values for five human samples with low analyte concentration has been determined with three reagent lots on two **cobas e** 411 analyzers with six runs distributed over a period of up to 5 days.

Samples were measured in one-fold determination in each run. In summary, 30 measuring points were collected per instrument, for a total of 60 measured values. The sum of standard deviations (SD total) of the five samples was calculated. The LoD was determined according to the following EP17-A2 calculation:

$$LoD = LoB + 1.653 \times SD_{total} \quad \text{(of low analyte samples)}$$

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510(k) Summary for the Elecsys CA 125 II assay, *continued*

Evaluations Summary, *continued*

Limit of Quantitation

LoQ of the Elecsys CA125 II assay was determined according to CLSI Guideline EP17-A2.

LoQ determines the lowest amount of analyte that can be quantitatively determined with stated accuracy and stated experimental conditions. The LoQ was determined as the lowest concentration of analyte which can be quantified with a total within-laboratory precision CV< 20%.

The distribution of values for three human sample pools each diluted to concentrations which covered the range between LoB and 2x LoQ has been determined with three reagent lot on two **cobas e** 411 analyzers with six runs distributed over three to five days. Each run was calibrated separately using a two point calibration.

Samples were measured in one-fold determination in each run. In summary, a total of 54 measuring points were collected per instrument, for a total of 108 measured values.

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510(k) Summary for the Elecsys CA 125 II assay, *continued*

Evaluations Summary, *continued*

Linearity

Linearity of the Elecsys CA125 II assay was assessed on the **cobas e** 411 immunoassay analyzer according to CLSI EP6-A.

Six dilution series were prepared from six different spiked human samples. The first three dilution series were performed with serum samples and the other three with plasma samples. Each dilution series included 15 dilutions. Each sample was measured 3-fold within one run and the measured concentrations were plotted against the expected sample concentration.

Dilution

The dilution study for the Elecsys CA125 II assay was performed on the **cobas e** 411 using three human samples spiked to analyte concentrations above the measuring range and diluted automatically. These measurements were compared against manual dilutions.

The samples were diluted with the Elecsys Diluent Universal. The diluted and undiluted samples were measured in triplicate.

Testing was performed on two **cobas e** 411 analyzers.

Percent recoveries were calculated between the median of the manual and automated dilution.

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510(k) Summary for the Elecsys CA 125 II assay, *continued*

Evaluations Summary, *continued*

High Dose Hook Effect

The high dose hook effect of the Elecsys CA125 II assay was assessed on the **cobas e** 411 analyzer

Two samples were spiked with analyte to a concentration of 50000U/mL. For each sample a dilution series was performed using Diluent Universal (Id. Nr. 175912) resulting in 5 to 6 samples above the measuring range. Each dilution was tested in single determination.

The hook concentration reported corresponds to the analyte concentration with a signal corresponding to at least 10% above the highest master calibrator.

HAMA Effect

The effect of the presence of human anti-mouse antibodies on the Elecsys CA125 II assay was assessed on the **cobas e** 411 analyzer

A specified HAMA serum and the related basic serum without interferent were spiked with the analyte to a concentration of 13.0 U/mL. These two samples were measured in duplicates.

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510(k) Summary for the Elecsys CA 125 II assay, *continued*

Evaluations Summary, *continued*

Endogenous Interference

The effect on quantitation of analyte in the presence of endogenous interfering substances using the Elecsys CA125 II was determined on the **cobas e** 411 analyzer for the following 5 interfering substances Intralipid, Biotin, Bilirubin, Rheumatic Factor and Hemolysis using three spiked human samples (one low, one medium, and one high) to prepare dilution series of 11 dilutions that were tested with one reagent lot.

Exogenous Interference

1) Drugs

   16 common and 23 additional pharmaceutical compounds were spiked into each of two human samples containing CA125 (low and high concentration). The spiked samples (spiked with 10.7 U/mL and 313 U/mL CA125) were evaluated at drug concentrations defined as 5- fold daily dose and tested for interference by the Elecsys CA125 II assay on **cobas e** 411 analyzer.

   Testing was performed in 3-fold determination with one reagent lot in one run on one **cobas e** 411 analyzer. The mean value is used to calculate the absolute deviation (U/mL, for samples ≤ 15 U/mL) and percentage deviation (%, for samples > 15 U/mL) of the drug sample to the reference.

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510(k) Summary for the Elecsys CA 125 II assay, *continued*

Evaluations Summary, *continued*

Exogenous Interference, *continued*

2) Anticoagulants

The effect on quantitation of analyte in the presence of anticoagulants with the Elecsys CA125 II assay was determined by comparing values obtained from native samples (single donors) drawn into Serum, Li-Heparin, K_2-EDTA-, K_3-EDTA-plasma primary tubes and Li-Heparin Plasma Separation Tubes.

51 or 52 serum/plasma pairs per sample material were tested in duplicates with one reagent lot on one **cobas e** 411 analyzer.

Potential effects are assessed by Passing/Bablok regression analyses.

Method Comparison

A method comparison was performed to evaluate the change in the sample/reagent ratio. The sample to reagent ratio has changed from 40 µL of sample and 60 µL of R1 and R2 on the formulation cleared under k972162 to 20µL of sample and 70 µL of R1 and R2 with the new assay. The method comparison proves the safety and effectiveness of the sample to reagent volumes has not affected the performance of the assay.

The study was performed on the Elecsys 2010 analyzer using the Elecsys CA125 II assay (sample/reagent ratios as cleared under k972162) and the CA125 II Cal Set (k003969)(X) against the Elecsys CA 125 II assay with the new sample/reagent ratios and the Elecsys CA125 II CalSet (k003969) (Y). A total of 80 human serum samples (all native single donors) with CA125 values from 4.7 –2680U/mL (X) and 4.8 –2594U/mL (Y) were measured in order to cover the entire measuring range.

Continued on next page

510(k) Summary for the Elecsys CA 125 II assay, *continued*

Evaluations Summary, *continued*

Method Comparison (CalSet)

A method comparison was performed using the Elecsys CA125 II assay in combination with the Elecsys CA125 II CalSet (cleared under K003969) as predicate device and in combination with the new cleared Elecsys CA125 II CalSet II (K140112).

The Elecsys CA125 II Assay is standardized against the Enzymun-Test CA 125 II method. This in turn was standardized against the CA 125 II RIA from Fujirebio Diagnostics.

The study was performed on the **cobas e** 411 analyzer using the Elecsys CA125 II assay with the CA125 II Cal Set(X) and the Elecsys CA 125II assay with the new Elecsys CA125 II CalSet II assay (Y)

A total of 111 human serum samples (all native single donors) with CA125 values from 3.19 –2621U/mL (X) and 4.05 –2641U/mL (Y) were measured in order to cover the entire measuring range.

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510(k) Summary for the Elecsys CA 125 II assay, *continued*

Evaluations Summary, *continued*

The reagent stability was performed in three different studies and they are:

Study 1: Reagent stability after first opening

Reagent stability after first opening for the Elecsys CA125 II assay was determined on a cobas e 411 analyzer by comparing the reagent stability for four kits of the same lot. All reagent kits were opened on day 0. One kit was placed on the analyzer and calibrated and reference values for the samples tested were determined.

The other three kits were stored at 2 to 8°C. After 5, 9 and 13 weeks, one of the stored kits was placed on the analyzer and calibrated, and the original test samples were measured.

Samples tested in duplicate include five human serum (HS) samples and two controls. The human serum samples used were native single donors.

Study 2: On-board reagent stability

On-board reagent stability for the CA125 II assay was tested on one **cobas e** 411 immunoassay analyzer. A fresh kit was placed on the analyzer and calibrated. Reference values for the samples tested were determined. After measurement, the kit was closed and kept at 20°C ± 3°C for 6 weeks to simulate on-board conditions. Measurements were repeated every week for nine weeks (64 days). The kit was placed on the analyzer again utilizing the calibration curve from seven days earlier for determinations of stability, and the original test samples were measured. The recovery was compared to the measurements from day zero. Samples were tested with one reagent lot in one run per day on one cobas e 411 analyzer in duplicate.

Samples tested included five human samples (pooled patient samples and single donor samples spiked with CA125) and two controls (PreciControl Tumormarker Level 1 and 2).

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510(k) Summary for the Elecsys CA 125 II assay, *continued*

Evaluations Summary, *continued*

Reagent Stability, *continued*

Study 3: Shelf life stability

In addition, real-time stability was used to determine CA125 II shelf-life stability.

In the real-time stability study, the CA125 II assay material was stored at 2 to 8°C. The stored assay reagents were tested at time point T=0 and at specified intervals over the shelf life of the device up to the planned shelf life plus one month. Testing was performed using PreciControl Tumor Marker 1 and 2 (stored at -20°C).

For the 154355-Lot, data for the time-points at 0, 9, 15 and 19 months were tested in duplicates. For the second and third lot (production lots 157240 and 158725) data for the time point at 0, 7, 13 and 19 months were tested in duplicates.

The average on-test recovery was calculated as percent recovery compared to the reference value (Assigned value for PreciControl Tumor Marker 1 and 2).

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510(k) Summary for the Elecsys CA 125 II assay, *continued*

Evaluations Summary, *continued*

The sample stability was performed with four different studies and they are:

Study 1: Sample stability at 2 to 8°C

Ten human samples for each sample type (Serum, K_2-EDTA-plasma, K_3-EDTA-plasma, Li-Heparin-plasma) were collected and stored at -80°C (reference).

After the first measurement (reference value), the samples were tested after storage at 2 to 8°C after 6 days.

Measurements were performed with three-fold determination on **cobas e** 411 analyzer. The median was used to calculate the percent recovery or absolute deviation to the reference value.

Study 2: Sample stability at room temperature

Ten human samples for each sample type (Serum, K_2-EDTA-plasma, K_3-EDTA-plasma, Li-Heparin-plasma) were collected and stored at -80°C (reference).

After the first measurement (reference value), the samples were tested after 9 hours at room temperature.

Measurements were performed with three-fold determination on **cobas e** 411 analyzer. The median was used to calculate the percent recovery or absolute deviation to the reference value.

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510(k) Summary for the Elecsys CA 125 II assay, *continued*

Evaluations Summary, *continued*

Sample Stability- *continued*

Study 3: Sample stability at -20°C
Ten human samples for each sample type (Serum, K_2-EDTA-plasma, K_3-EDTA-plasma, Li-Heparin-plasma) were measured fresh (reference) and after storage at -20°C for 25 weeks.

Measurements were performed with three-fold determination on **cobas e** 411 analyzer. The median was used to calculate the percent recovery or absolute deviation to the reference value.

Study 4: Sample stability through freeze/thaw cycles
Ten human samples for each sample type (Serum, K_2-EDTA-plasma, K_3-EDTA-plasma, Li-Heparin-plasma) were collected and stored at -80°C (reference).

After the first measurement (reference value), the samples were tested after 4 freeze/thaw cycles.

Measurements were performed with three-fold determination on **cobas e** 411 analyzer. The median was used to calculate the percent recovery or absolute deviation to the reference value.

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510(k) Summary for the Elecsys CA 125 II assay, *continued*

Evaluations Summary, *continued*

Calibration Stability was performed with two different studies and they are:

Study 1: Lot calibration stability:
The stability of lot calibration was determined by comparing the calibration for four kits of the same lot. On day 0, the first reagent kit was opened and calibrated, and samples were measured. The same samples were also measured with fresh opened kits of the same lot, using the same calibration established by the first kit, after 5 and 9 weeks on one **cobas e** 411.

Four human serum samples (pooled patient samples spiked with CA125) and two controls were measured in duplicate with one reagent lot in one run per day.

Study 2: On-board calibration stability:
On-board calibration stability for the ElecsysCA125 II assay was tested on one **cobas e** 411 analyzer. One reagent kit was opened and samples were measured on day 0. The same samples were then retested after 8 days with a new opened reagent bottle kept at 20±3°C (on-board condition) using the calibration from day 1. Recovery was calculated based on the initial values.

Five human serum samples (pooled patient samples and single donor samples spiked with CA125 II) and two controls were tested in duplicate with one reagent lot on one **cobas e** 411 in one run per day.

Continued on the next page

510(k) Summary for the Elecsys CA 125 II assay, *continued*

Evaluations Summary, *continued*

Recovey of Controls
A set of PreciControl Tumor Marker was evaluated in duplicate with one reagent lot on two **cobas e 411** analyzers. Two runs were performed on each analyzer. The results were compared against the target ranges of the PreciControl Tumor Marker.

The measuring range is defined to meet CLSI guideline EP17-A2 requirements.

Performance Characteristics of CA 125 II CalCheck
The Elecsys CA 125 II Calcheck was evaluated for value assignment and stability.

Conclusion

Based on performance data described above the Elecsys CA 125 II assay and CA 125 II CalCheck devices were found to have safety and effectiveness profiles similar to the predicate devices.