



Food and Drug Administration
10903 New Hampshire Avenue
Document Control Center – WO66-G609
Silver Spring, MD 20993-0002

Roche Diagnostics
Angelo Pereira
Regulatory Affairs Senior Program Manager
9115 Hague Rd
Indianapolis, IN 46250

July 28, 2016

Re: K160910
Trade/Device Name: Elecsys Syphilis
Regulation Number: 21 CFR 866.3830
Regulation Name: *Treponema pallidum* treponemal test reagents
Regulatory Class: II
Product Code: LIP
Dated: July 22, 2016
Received: July 25, 2016

Dear Mr. Pereira:

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,

Tamara V. Feldblyum -S for

Uwe Scherf, M.Sc., Ph.D.
Director
Division of Microbiology Devices
Office of In Vitro Diagnostics
and Radiological Health
Center for Devices and Radiological Health

Enclosure

Indications for Use

510(k) Number (if known)
K160910

Device Name
Elecsys Syphilis
PeciControl Syphilis

Indications for Use (Describe)

Immunoassay for the *in vitro* qualitative detection of total antibodies (IgG and IgM) to *Treponema pallidum* in human serum and plasma. The test is intended as an aid in the diagnosis of syphilis infection in conjunction with clinical signs and symptoms.

The Elecsys Syphilis immunoassay is not intended for use in screening blood or tissue donors. The effectiveness of this assay in testing blood or tissue donors has not been established.

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

PeciControl Syphilis is intended for the quality control of the Elecsys Syphilis immunoassay on the cobas e 411 analyzer.

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.

This section applies only to requirements of the Paperwork Reduction Act of 1995.

DO NOT SEND YOUR COMPLETED FORM TO THE PRA STAFF EMAIL ADDRESS BELOW.

The burden time for this collection of information is estimated to average 79 hours per response, including the time to review instructions, search existing data sources, gather and maintain the data needed and complete and review the collection of information. Send comments regarding this burden estimate or any other aspect of this information collection, including suggestions for reducing this burden, to:

Department of Health and Human Services
Food and Drug Administration
Office of Chief Information Officer
Paperwork Reduction Act (PRA) Staff
PRASStaff@fda.hhs.gov

"An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB number."

Elecsys Syphilis

510(k) Summary

This summary of 510(k) safety and effectiveness information is being submitted in accordance with the requirements of 21 CFR 807.92.

Submitter Name	Roche Diagnostics
Address	9115 Hague Road P.O. Box 50416 Indianapolis, IN 46250-0416
Contact	Angelo Pereira Phone: (317) 521-3544 FAX: (317) 521-2324 Email: angelo.pereira@roche.com
Date Prepared	July 21, 2016
Proprietary Name	Elecsys Syphilis
Common Name	Syphilis assay
Classification Name	<i>Treponema pallidum</i> treponemal test reagent
Product Codes	Product Code: LIP; 21CFR866.3830
Predicate Devices	Immulite 2000 Syphilis Screen test system, K091361
Establishment Registration	For Elecsys Syphilis, the establishment registration number for Roche Diagnostics GmbH in Mannheim, Germany is 9610126, and for Penzberg, Germany, 9610529. The establishment registration number for Roche Diagnostics in the United States is 1823260.

1. DEVICE DESCRIPTION

The Elecsys Syphilis assay is a fully automated qualitative assay detecting IgG and IgM antibodies to *Treponema pallidum*, the causative agent of syphilis. Assay results, in conjunction with other laboratory results and clinical information, may be used to provide presumptive

evidence of active or previous infection with *Treponema pallidum* in persons with signs and symptoms of syphilis, as well as in patients at risk for syphilis infection. This assay does not determine the stage of infection or associated disease.

PreciControl Syphilis is a lyophilized control based on human serum. It is used for monitoring the accuracy of the Elecsys Syphilis immunoassay.

2. INTENDED USE

Elecsys Syphilis:

Immunoassay for the *in vitro* qualitative determination of total antibodies (IgG and IgM) to *Treponema pallidum* in human serum and plasma. The test is intended as an aid in the diagnosis of syphilis infection in conjunction with clinical signs and symptoms.

The Elecsys Syphilis immunoassay is not intended for use in screening blood or tissue donors. The effectiveness of this assay in testing of blood and tissue donors has not been established.

The electrochemiluminescence immunoassay “ECLIA” is intended for use on the **cobas e 411** analyzer.

PreciControl Syphilis:

PreciControl Syphilis is intended for the quality control of the Elecsys Syphilis immunoassay on **cobas e 411** analyzer.

3. TECHNOLOGICAL CHARACTERISTICS

The Elecsys Syphilis assay is a qualitative assay that uses the established double antigen sandwich format. Biotinylated *T. pallidum*-specific recombinant antigens (TpN15, TpN17 and

TpN47) and *T. pallidum*-specific recombinant antigens (TpN15, TpN17 and TpN47) labeled with a ruthenium complex react with anti *T. pallidum*-specific antibodies to form a sandwich complex. The assay uses monomeric and polymeric antigens, ensuring the detection of both IgG and IgM anti-treponemal antibodies. After addition of streptavidin-coated microparticles, the complex becomes bound to the solid phase via interaction of biotin and streptavidin. The reaction mixture is aspirated into the measuring cell where the microparticles are magnetically bound onto the surface of the electrode. Unbound substances are then removed with ProCell. Application of a voltage to the electrode then induces chemiluminescent emission which is measured by a photomultiplier.

The predicate device is a solid phase, one-step chemiluminescent enzyme immunoassay. The solid phase (bead) is coated with purified recombinant *T. pallidum* 17 (Tp17) antigen. The liquid phase consists of alkaline phosphatase (bovine calf intestine) conjugated to purified recombinant *T. pallidum* 17 (Tp17) antigen.

Patient sample and the reagent are incubated together with the coated bead. During this time, total antibody to *T. pallidum* in the sample forms the antigen sandwich complex with purified recombinant *T. pallidum* 17 (Tp17) antigen on the bead and enzyme conjugated purified recombinant *T. pallidum* 17 (Tp17) antigen in the reagent. Unbound patient sample and enzyme conjugate are then removed by centrifugal washes. Finally, chemiluminescent substrate is added to the reaction tube containing the bead and the signal is generated in proportion to the bound enzyme.

Both the predicate device and Elecsys Syphilis provide prepackaged reagents, calibrators and controls for use on automated test systems. A comparison of the important similarities and differences of these assays is provided in the following table:

Table of similarities and differences

Parameter	New Device	Predicate
Intended Use	<p>Immunoassay for the <i>in vitro</i> qualitative determination of total antibodies (IgG and IgM) to <i>Treponema pallidum</i> in human serum and plasma. The test is intended as an aid in the diagnosis of syphilis infection in conjunction with clinical signs and symptoms.</p> <p>The Elecsys Syphilis assay is not intended for use in screening blood or plasma donors.</p> <p>The electrochemiluminescence immunoassay "ECLIA" is intended for use on cobas e 411 analyzer</p>	<p>The IMMULITE 2000 Syphilis Screen test is a treponemal testing procedure for the qualitative detection of antibodies to <i>Treponema pallidum</i> in human serum or heparinized plasma on the IMMULITE 2000 analyzer as an aid in the diagnosis of syphilis.</p> <p>The IMMULITE 2000 Syphilis Screen test is not intended for use in screening blood or plasma donors.</p>
Analytes measured	Antibodies to <i>Treponema pallidum</i>	same
Instrument	Cobas e 411	IMMULITE 2000 Systems
Measurement	Qualitative	same
Antigens used	Recombinant antigens TpN17, TpN15 and TpN47	Recombinant antigen Tp17
Cut-off	<p><1.00 Non-reactive</p> <p>≥1.00 Reactive</p>	<p><0.9 Non-reactive</p> <p>≥0.9 to <1.1 Indeterminate</p> <p>≥1.1 Reactive</p>
Sample type	Serum, K ₂ EDTA, K ₃ EDTA, CPDA, NaCitrate and Li Heparin	Serum, heparinized plasma
Assay type	Double antigen sandwich electrochemiluminescence immunoassay	Enzyme labeled, one-step chemiluminescent immunoassay

4. NON-CLINICAL PERFORMANCE EVALUATION

Precision

Precision was evaluated with serum samples on a single cobas e 411 Immunoassay Analyzer according to CLSI guideline EP5-A2. One reagent lot was evaluated. The protocol was performed by testing 2 controls (PeciControl 1 and PeciControl 2) and 6 human sera (HS) (negative, near cut-off, positive) in duplicate per run, 2 runs per day for 21 days. The samples were run in randomized order on the analyzer.

Sample	Mean [COI]	Repeatability		Intermediate precision		n
		SD [COI]	CV [%] (UCL * 95%)	SD [COI]	CV [%] (UCL * 95%)	
HS negative 1	0.103	0.002	1.6 (2.0)	0.003	3.2 (4.1)	84
HS negative 2	0.821	0.0174	2.1 (2.7)	0.019	2.3 (2.7)	84
HS positive 1	1.01	0.028	2.8 (3.5)	0.033	3.2 (3.9)	84
HS positive 2	1.12	0.018	1.6 (2.1)	0.022	1.9 (2.3)	84
HS positive 3	9.99	0.171	1.7 (2.2)	0.262	2.6 (3.2)	84
HS positive 4	50.2	0.986	2.0 (2.5)	1.24	2.5 (3.0)	84
PreciControl 1	0.106	0.003	2.4 (3.1)	0.004	4.1 (5.1)	84
PreciControl 2	4.95	0.101	2.1 (2.6)	0.161	3.2 (4.1)	84

Endogenous Interferences

Interference by endogenous substances was evaluated at three anti-*T. pallidum* antibody concentrations (negative, near cut-off and positive). Each serum pool was spiked with the interferent to the levels indicated in the table below.

	Interfering substance measured up to	No interference seen up to	Label Claim
Intralipid® (Lipemia)	2000 mg/dL	2000 mg/dL	2000 mg/dL
Biotin	70 ng/mL	70 ng/mL	60 ng/mL
Bilirubin	66 mg/dL	66 mg/dL	66 mg/dL
Hemoglobin	1000 mg/dL	1000 mg/dL	500 mg/dL
Rheumatoid Factor	1500 IU/mL	1500 IU/mL	1500 IU/mL
human serum albumin	10 g/dL	10 g/dL	10 g/dL
human IgG	7.0 g/dL	6.3 g/dL	32 g/L
human IgM	1.0 g/dL	1.0 g/dL	10 g/L
human IgA	7.0 g/dL	2.8 g/dL	2.8 g/dL

Drug interferences

16 pharmaceutical compounds were spiked into human serum samples at three anti-*T. pallidum* antibody concentrations (negative, low-positive, high positive) and tested with the Elecsys Syphilis assay on the **cobas e 411** analyzer. The concentration of the spiked aliquots was determined in 3-fold determination and compared to the anti-*T. pallidum* antibody concentration

determined for the reference aliquot (also in 3-fold determination) on one **cobas e 411** analyzer. No interference was observed at the levels shown in the table below.

Drug tested	Conc. of spiked drug tested (mg/L)
Acetylcystein	150
Ampicillin-Na	1000
Ascorbic acid	300
Cyclosporine	5
Cefoxitin	2500
Heparin	5000 U/L
Levodopa	20
Methyldopa +1.5	20
Metronidazole	200
Phenylbutazone	400
Doxycyclin	50
Acetylsalicylic Acid	1000
Rifampicin	60
Acetaminophen	200
Ibuprofen	500
Theophylline	100

Serum Plasma Matrix comparison

The effect of anticoagulants on the Elecsys Syphilis Immunoassay was determined by comparing values obtained from native samples spiked with anti-*T. pallidum* antibody (single donors) drawn into serum and plasma tubes.

The data support the package insert claim that serum, serum separation tubes, Li-Heparin plasma tubes, K2-EDTA- and K3-EDTA-plasma, Na Citrate and CPDA plasma specimens are acceptable sample types for use with the Elecsys Syphilis assay.

Analytical specificity

The analytical specificity of the Elecsys Syphilis assay was determined using human serum samples (single donors, native) spiked with potential cross-reactant antibodies.

6. CLINICAL PERFORMANCE

Reproducibility

A reproducibility study was conducted following CLSI EP5-A2 at three sites incorporating a 7 member panel consisting of 5 serum pools (high negative, low positive and moderately positive) and 2 controls that were assayed for 5 days, 2 runs per day, 3 replicates per run. Data from all three sites were combined to achieve SD and percent CV for repeatability (within-run), between run, between-day, between site and reproducibility. The overall reproducibility (imprecision) data are summarized in the following table:

Sample	N	Mean		Within Run Repeatability			Between Run		Between Day		Between Site		Reproducibility		
		COI	SD	95% CI	% CV	SD	% CV	SD	% CV	SD	% CV	SD	95% CI	% CV	
HSP 06	90	1.02	0.01	(0.01, 0.01)	1.16	0.02	2.28	0.00	0.00	0.01	1.29	0.03	(0.02, 0.04)	2.86	
HSP 07	90	1.13	0.02	(0.02, 0.03)	1.90	0.03	2.57	0.00	0.00	0.01	0.79	0.04	(0.03, 0.05)	3.29	
HSP 08	90	0.94	0.01	(0.01, 0.02)	1.58	0.02	2.55	0.00	0.00	0.01	0.75	0.03	(0.02, 0.04)	3.09	
HSP 09	90	0.85	0.02	(0.01, 0.02)	1.88	0.02	2.49	0.00	0.00	0.01	1.23	0.03	(0.02, 0.04)	3.36	
HSP 10	90	3.24	0.09	(0.08, 0.11)	2.78	0.08	2.61	0.00	0.00	0.00	0.00	0.12	(0.11, 0.15)	3.82	
SYPH PC1	90	0.12	0.00	(0.00, 0.00)	2.41	0.00	2.39	0.00	1.15	0.01	4.47	0.01	(0.00, 0.02)	5.73	
SYPH PC2	90	4.76	0.08	(0.07, 0.10)	1.65	0.14	2.89	0.00	0.00	0.03	0.70	0.16	(0.13, 0.21)	3.40	

Clinical performance in prospective cohorts

A total of 2282 prospectively collected samples of the intended use population were tested at 3 sites using the Elecsys Syphilis assay, including 1524 subjects for routine syphilis testing, 457 HIV positive subjects and 301 pregnant women. In addition, all samples were tested according to a composite algorithm using FDA-cleared tests that included the predicate Syphilis immunoassay, the Rapid Plasma Reagin (RPR) non-treponemal specific assay and the *Treponema pallidum* Particle Agglutination, treponemal-specific assay.

The following table summarizes the performance of Elecsys Syphilis compared with the final comparator results for all prospective cohorts.

Elecsys Syphilis compared with Final Comparator for all prospective cohorts

	Final Comparator Results		
Elecsys Syphilis	Positive for Syphilis	Negative for Syphilis	Total
Reactive	228	16	244
Non reactive	0	2038	2038
Total	228	2054	2282

Percent agreement by category for prospective cohorts

Cohort	Positive Percent Agreement		PPA 95 % CI	Negative Percent Agreement		NPA 95 % CI
	%	Ratio		%	Ratio	
Routine Syphilis	100	66/66	94.56 to 100.00	99.8	1455/1458	99.40 to 99.96
HIV	100	162/162	97.75 to 100.00	95.6	282/295	92.58 to 97.63
Pregnant	N/A	0/0	N/A	100	301/301	98.78 to 100.00
Total	100	228/228	98.40 to 100.00	99.2	2038/2054	98.74 to 99.55

Clinical performance in retrospective medically diagnosed individuals

Clinical performance in the pre-selected retrospective cohort included a total of 169 specimens, including 15 pregnant positive women and 154 subjects medically diagnosed with syphilis at different stages. The comparison between the Elecsys Syphilis results and the final comparator results is given in the following table.

Elecsys Syphilis compared with Final Comparator for retrospective cohorts

	Final Comparator Results		
Elecsys Syphilis	Positive for Syphilis	Negative for Syphilis	Total
Reactive	155	0	155
Non-reactive	2	12	14
Total	157	12	169

Percent agreement by category for retrospective cohorts

Cohort	Positive Percent Agreement		PPA 95 % CI	Negative Percent Agreement		NPA 95 % CI
	%	Ratio		%	Ratio	
Pregnant (Retrospective)	100	15/15	78.20 to 100.00	N/A	0/0	N/A
Staged	98.6	140/142	95.00 to 99.83	100	12/12	73.54 to 100.00
Overall (Retrospective)	98.7	155/157	95.47 to 99.85	100	12/12	73.54 to 99.55

Clinical performance in pregnant women

A total of 316 pregnant female samples were tested in the study. Of these, 301 were prospectively collected and 15 were retrospectively collected. The percent agreement between the Elecsys Syphilis results and the final comparator results is shown below, stratified by pregnancy trimesters compared with the Composite Algorithm for pregnant women:

Percent agreement of Elecsys Syphilis with final comparator results for Pregnant Women

Cohort	Positive Percent Agreement		PPA 95 % CI	Negative Percent Agreement		NPA 95 % CI
	%	Ratio		%	Ratio	
Pregnant (Prospective)	N/A	0/0	N/A	100	301/301	98.78 to 100.00
1 st Trimester	N/A	0/0	N/A	100	100/100	96.38 to 100.00
2 nd Trimester	N/A	0/0	N/A	100	125/125	97.09 to 100.00
3 rd Trimester	N/A	0/0	N/A	100	76/76	95.26 to 100.00
Pregnant (Retrospective)	100	15/15	78.20 to 100.00	N/A	0/0	N/A
1 st Trimester	100	7/7	59.04 to 100.00	N/A	0/0	N/A
3 rd Trimester	100	8/8	63.06 to	N/A	0/0	N/A

Cohort	Positive Percent Agreement		PPA 95 % CI	Negative Percent Agreement		NPA 95 % CI
	%	Ratio		%	Ratio	
			100.00			

Clinical performance in Medically Diagnosed Individuals

Samples were collected from 154 individuals diagnosed with primary, secondary or latent syphilis. They included 10 females and 144 males. Results of the Elecsys Syphilis assay for this cohort are summarized below.

Reactivity of Elecsys Syphilis in subjects medically diagnosed with syphilis

Syphilis stage	Treatment status	N	Elecsys Syphilis Results	
			Reactive	Non-reactive
Primary	Treated	29	16	13*
	Untreated	25	25	0
Secondary	Treated	25	24	1
	Untreated	25	25	0
Latent	Treated	25	25	0
	Untreated	25	25	0

* 12 of these samples also tested negative for Syphilis with the composite testing algorithm

Performance in apparently healthy individuals

Specimens were collected from 209 apparently healthy individuals. Of these, 80 were female and 129 male. The results of the Elecsys Syphilis assay for this cohort are shown below

	Elecsys Syphilis Results		
	Reactive	Non-reactive	
	N	N	
Female	9 (11.3 %)	71 (88.7 %)	80
Male	11 (8.5 %)	118 (91.5 %)	129
Total	20 (9.6 %)	189 (90.4 %)	209

Expected values

In this clinical study there were 2282 prospectively collected specimens for the intended use population that were tested with the Elecsys Syphilis assay. There were 244 reactive samples for a 10.7% prevalence of *T. pallidum* antibodies in the study population. The distribution of the Elecsys Syphilis reactive and non-reactive results is summarized below by age and gender.

Age Range (years)	Gender	Elecsys Syphilis Results		
		Reactive	Non-reactive	Total
18 21	Female	0 (0.00 %)	247 (100 %)	247
	Male	6 (3.5 %)	165 (96.5 %)	171
22 29	Female	0 (0.00 %)	358 (100 %)	358
	Male	19 (10.7 %)	159 (89.3 %)	178
30 39	Female	10 (3.7 %)	261 (96.3 %)	271
	Male	13 (12.3 %)	93 (87.7 %)	106
40 49	Female	29 (12.1 %)	210 (87.9 %)	239
	Male	29 (20.0 %)	116 (80.0 %)	145
50 59	Female	47 (20.8 %)	179 (79.2 %)	226
	Male	55 (27.1 %)	148 (72.9 %)	203
60 69	Female	11 (23.9 %)	35 (76.1 %)	46
	Male	23 (29.5 %)	55 (70.5 %)	78
70 79	Female	0 (0.00 %)	5 (100 %)	5
	Male	2 (22.2 %)	7 (77.8 %)	9
Combined	Total	244 (10.7 %)	2038 (89.3 %)	2282

7. CONCLUSIONS

There was good agreement between the Elecsys Syphilis assay and the results from the final comparator algorithm.

A comparison of the device features, intended use, non-clinical and clinical data supports a decision that Elecsys Syphilis is substantially equivalent to the predicate assay.