Roche Diagnostics
Bin Sun
Regulatory Affairs Program Manager
9115 Hague Road
Indianapolis, Indiana 46250

Re: K211302
Trade/Device Name: Elecsys Syphilis
Regulation Number: 21 CFR 866.3830
Regulation Name: Treponema pallidum treponemal test reagents
Regulatory Class: Class II
Product Code: LIP, JJX
Dated: April 28, 2021
Received: April 29, 2021

Dear Bin Sun:

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. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database located at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm identifies combination product submissions. 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 Part

801 and Part 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803) for devices or postmarketing safety reporting (21 CFR 4, Subpart B) for combination products (see https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

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 https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance) and CDRH Learn (https://www.fda.gov/training-and-continuing-education/cdrh-learn). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/contact-us-division-industry-and-consumer-education-dice) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Maria Garcia, Ph.D.
Branch Chief
Division of Microbiology Devices
OHT7: Office of In Vitro Diagnostics
and Radiological Health
Office of Product Evaluation and Quality
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: 06/30/2023
See PRA Statement below.

510(k) Number *(if known)*

K211302

Device Name
Elecsys 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 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)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

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

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Date Prepared	April 28, 2021
Proprietary Name	Elecsys Syphilis
Common Name	Syphilis assay
Classification Name	*Treponema pallidum* treponemal test reagent
Product Codes, Regulation Numbers	Product Code: LIP; 21CFR866.3830
Predicate Devices	Elecsys Syphilis (K160910)
Establishment Registration	Roche Diagnostics GmbH Mannheim, Germany: 9610126 Roche Diagnostics GmbH Penzberg, Germany: 9610529 Roche Diagnostics Indianapolis, IN United States: 1823260.

1. DEVICE DESCRIPTION

The Elecsys Syphilis immunoassay is a fully automated, qualitative assay that uses a double antigen sandwich format for the detection of IgM and IgG antibodies to *T. pallidum*.

Recombinant *T. pallidum* antigens labeled with either biotin or a ruthenium complex bind to *T. pallidum*-specific IgG or IgM to form a double antigen sandwich complex. The sandwich complex binds to streptavidin-coated microparticles which can be immobilized magnetically to the surface of an electrode. Unbound substances are removed during a wash step using ProCell. A chemiluminescent substrate is then added to the reaction tube. Application of a voltage to the electrode induces a chemiluminescent emission which is measured by a photomultiplier.

The presence or absence of anti-TP antibodies in the specimen is determined by comparing the chemiluminescent signal in the reaction to the cutoff index (COI) determined from an active calibration. The strength of the signal generated is proportional to the amount of bound conjugate and thus the amount of anti-*T. pallidum* antibodies present in the specimen. If the chemiluminescent signal in the reaction is greater than or equal to the cutoff signal, the specimen is considered reactive for anti-TP antibodies. If the chemiluminescent signal is below the cutoff signal, the specimen is considered nonreactive for the anti-TP antibodies.

The results are printed out as follows:

COI ≥ 1.00	Reactive
COI < 1.00	Nonreactive

Interpretation of results:

Reactive	Reactive for treponemal antibodies
Nonreactive	Nonreactive for treponemal antibodies

Test results are intended to aid in diagnosis only. As with all serological tests for syphilis, results should always be interpreted in conjunction with additional treponemal or non-treponemal serologic test results (as appropriate), the patient's clinical symptoms, medical history, and other clinical and/or laboratory findings to produce a diagnosis of syphilis by disease stage.

All initially reactive samples should be retested in duplicate with the Elecsys Syphilis assay. If cutoff index values < 1.00 are found in both cases, the samples are considered negative for *anti-Treponema pallidum* antibodies.

Initially reactive samples with cutoff index values of ≥ 1.00 in either of the retests are considered repeatedly reactive. Repeatedly reactive samples must be confirmed according to recommended confirmatory algorithms.

The PreciControl Syphilis 1 and 2 controls and Syphilis Cal1 and Cal2 calibrators are for use with the Elecsys Syphilis Assay.

The reagent working solutions include:

- M Streptavidin-coated microparticles, 1 bottle, 14.1 mL:
  Streptavidin-coated microparticles 0.72 mg/mL; preservative.
- R1 TP-specific recombinant antigens (E. coli)~biotin, 1 bottle, 19.7 mL:
  Biotinylated TP-specific recombinant antigens (E. coli) 0.7 mg/L; MES[a)] buffer 50 mmol/L, pH 6.5; preservative.
- R2 TP-specific recombinant antigens (E. coli)~$Ru(bpy)_3^{2+}$, 1 bottle, 19.7 mL:
  TP specific recombinant antigens labeled with ruthenium complex 0.7 mg/L; MES buffer 50 mmol/L, pH 6.5; preservative.

a) MES = 2-morpholino-ethane sulfonic acid

- Cal1 Negative calibrator 1 (lyophilized), 1 bottle for 1.0 mL:
  Human serum, non-reactive for anti TP antibodies; preservative.
- Cal2 Positive calibrator 2 (lyophilized), 1 bottle for 1.0 mL:
  Human serum, reactive for anti TP antibodies; preservative.

2. INDICATIONS FOR USE

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 **e**lectro**c**hemi**l**uminescence **i**mmuno**a**ssay "ECLIA" is intended for use on **cobas e** immunoassay analyzers.

3. TECHNOLOGICAL CHARACTERISTICS

The following table compare the Elecsys Syphilis with its predicate device, Elecsys Syphilis (K160910).

Technical Characteristics Comparison Table between Current Elecsys Syphilis and the Updated Elecsys Syphilis Immunoassay

Feature	Candidate Device Updated Elecsys Syphilis	Predicate Device Elecsys Syphilis (K160910)
Intended Use	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 **cobas e** analyzer.	Same
Assay Method	Double antigen sandwich assay	Same
Detection Method	Electrochemiluminescence (ECLIA)	Same
Instrument Platform	**cobas e** 801	Same
Test Time	18 min	Same
Test Type	Qualitative	Same

Feature	Candidate Device Updated Elecsys Syphilis	Predicate Device Elecsys Syphilis (K160910)
Sample material	Serum collected using standard sampling tubes or tubes containing separating gel. Li-heparin, Na-heparin, K_2-EDTA, K_3-EDTA, CPDA and Na-citrate plasma. Li-heparin plasma tubes containing separating gel can be used.	Same
Biotin tolerance	≤ 1200 ng/mL	≤ 60 ng/mL
Calibration	2-point	Same
Controls	PreciControl Syphilis	Same

4. NON-CLINICAL PERFORMANCE EVALUATION

A limited number of studies were conducted to verify the assay performance cleared under K160910 was not affected by the changes made to improve tolerance to elevated levels of biotin. The following performance data are provided in support of the substantial equivalence determination:

- Precision according to CLSI EP5-A3
- Biotin interference study according to CLSI EP07-A3
- Matrix Comparison with clinical samples
- Reagent and calibration stability studies
- Lot calibration stability

All performance specifications were met.

4.1. Precision

The precision of the Elecsys Syphilis assay was evaluated on one **cobas e** 801 immunoassay analyzer with one reagent lot. The protocol consisted of testing 2 aliquots of each of two levels of controls and 7 human serum samples per run, 2 runs per day for 21 days. The samples were run in randomized order on the analyzer. Repeatability and Intermediate imprecision were

calculated according to CLSI EP05-A3 including the 95% confidence interval and a summary of the results is shown below.

cobas e 801 analyzer					
		Repeatability		**Intermediate precision**	
Sample	Mean COI	SD COI	CV %	SD COI	CV %
HS[1)], negative 1	0.125	0.00192	1.5	0.00210	1.7
HS, negative 2	0.888	0.0175	2.0	0.0264	3.0
HS, positive 1	1.09	0.0173	1.6	0.0260	2.4
HS, positive 2	4.11	0.0983	2.4	0.126	3.1
HS, positive 3	6.88	0.198	2.9	0.249	3.6
HS, positive 4	15.8	0.395	2.5	0.574	3.6
HS, positive 5	16.4	0.395	2.4	0.540	3.3
PC[2)] Syphilis 1	0.0951	0.00107	1.1	0.00130	1.4
PC Syphilis 2	5.90	0.126	2.1	0.155	2.6

1) HS = human serum

2) PC = PreciControl

4.2. Biotin Interference

The effect on quantitation of analyte in the presence of biotin using the updated Elecsys Syphilis assay was determined using three serum samples (negative, close to cut-off, positive) according to CLSI EP07-A3 Appendix A.

One aliquot of each serum sample was spiked with the interfering substance (biotin), another aliquot was spiked with the same volume of the respective solvent (dilution pool). The interfering pool was then incrementally diluted into the dilution pool. The recovery for each sample was calculated by comparison to the analyte concentration of the respective dilution pools.

For samples “close to cut-off” and “low positive”, samples were prepared by pooling native serum samples with high and low concentrations.

The maximum value with no interference observed was 2400 ng/mL. The claim of the Instruction for Use will be set to ≤ 1200 ng/mL.

4.3. Method Comparison to Predicate

A method comparison was performed using the Elecsys Syphilis updated assay (candidate device) and the current Elecsys Syphilis immunoassay (predicate device) to assess the bias between the two assays. A total of 232 samples from the intended use population were measured with one reagent lot of the current assay and three different reagent lots of the updated assay in single determination on the **cobas e** 801 analyzer covering the entire measuring range. From these measurements, Positive Agreement and Negative Agreement between the current and updated assay were calculated. The resulting data support the equivalence of the current non-biotin and biotin-updated assay.

4.4. Stability

The stability studies and acceptance criteria have been reviewed and found to be acceptable. The stability data supports Roche Diagnostic's claims as reported in the package labeling.

5. ADDITIONAL INFORMATION

The Elecsys Syphilis is intended to be used with the following calibrators and controls:

- Syphilis Cal1 and Syphilis Cal2, which is included in the kit
- PreciControl Syphilis

There have been no changes to these items marketed with the new Elecsys Syphilis immunoassay.

PreciControl Syphilis, product code JJX, is a Class I 510(k) Exempt device; therefore, it is not included with this submission.

6. CONCLUSIONS

The information provided in this 510(k) Premarket Notification is complete and supports a substantial equivalence decision. The data from the analytical studies demonstrate that the device

is as safe, as effective, and performs as well as the legally marketed predicate device with improved biotin tolerance level up to 1200 ng/mL.