I Background Information:

A 510(k) Number

K211302

B Applicant

Roche Diagnostics

C Proprietary and Established Names

Elecsys Syphilis

D Regulatory Information

<table>
<thead>
<tr>
<th>Product Code(s)</th>
<th>Classification</th>
<th>Regulation Section</th>
<th>Panel</th>
</tr>
</thead>
<tbody>
<tr>
<td>LIP</td>
<td>Class II</td>
<td>21 CFR 866.3830 - Treponema Pallidum Treponemal Test Reagents</td>
<td>MI - Microbiology</td>
</tr>
</tbody>
</table>

II Submission/Device Overview:

A Purpose for Submission:

Market clearance for a previously cleared assay to detect antibodies to *T. pallidum* in human serum and plasma that has been modified to improve tolerance to elevated levels of biotin.

B Measurand:

Antibodies to *T. pallidum* (IgM and IgG)

C Type of Test:

A qualitative double antigen sandwich electrochemiluminescence immunoassay.
III Intended Use/Indications for Use:

A Intended Use(s):
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.

B Indication(s) for Use:
Same as Intended Use

C Special Conditions for Use Statement(s):
Rx - For Prescription Use Only

D Special Instrument Requirements:
For use with the cobas e 801.

IV Device/System Characteristics:

A 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 (TP). 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 enzyme 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 reported out as follows:

COI ≥ 1.00 Reactive
COI < 1.00 Nonreactive
Interpretation of results:

<table>
<thead>
<tr>
<th>Reactive</th>
<th>Reactive for treponemal antibodies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nonreactive</td>
<td>Nonreactive for treponemal antibodies</td>
</tr>
</tbody>
</table>

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-\textit{Treponema pallidum} antibodies.

Initially reactive samples with cutoff index values of \( \geq 1.00 \) 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.

**B Principle of Operation:**

This is a fully automated electrochemiluminescence immunoassay.

**V Substantial Equivalence Information:**

**A Predicate Device Name(s):**
Elecsys Syphilis

**B Predicate 510(k) Number(s):**
K160910

**C Comparison with Predicate(s):**

<table>
<thead>
<tr>
<th>Device &amp; Predicate Device(s):</th>
<th>K211302</th>
<th>K160910</th>
<th>Change Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Device Trade Name</td>
<td>Elecsys Syphilis</td>
<td>Elecsys Syphilis</td>
<td></td>
</tr>
<tr>
<td>General Device Characteristic</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Similarities</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intended Use/Indications For Use</td>
<td>Same</td>
<td></td>
<td>Immunoassay for the in vitro qualitative detection of total antibodies (IgG and IgM) to \textit{Treponema pallidum} in human serum</td>
</tr>
</tbody>
</table>
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.

<table>
<thead>
<tr>
<th>Assay Method</th>
<th>Same</th>
<th>Double antigen sandwich assay</th>
<th>N/A</th>
</tr>
</thead>
<tbody>
<tr>
<td>Detection Method</td>
<td>Same</td>
<td>Electrochemiluminescence (ECLIA)</td>
<td>N/A</td>
</tr>
<tr>
<td>Instrument Platform</td>
<td>cobas e 801</td>
<td>cobas e 411, e 601, e 602, and e 801</td>
<td>Initially limited to use on the cobas e 801 analyzer</td>
</tr>
<tr>
<td>Test Time</td>
<td>Same</td>
<td>18 minutes</td>
<td>N/A</td>
</tr>
<tr>
<td>Test Type</td>
<td>Same</td>
<td>Qualitative</td>
<td>N/A</td>
</tr>
<tr>
<td>Specimen matrices</td>
<td>Same</td>
<td>Serum, Li-heparin, Na-heparin, K2-EDTA, K3-EDTA, CPDA and Na-citrate plasma</td>
<td>N/A</td>
</tr>
<tr>
<td><strong>General Device</strong></td>
<td><strong>Characteristic</strong></td>
<td><strong>Differences</strong></td>
<td></td>
</tr>
<tr>
<td>Biotin Tolerance</td>
<td>( \leq 1200 \text{ ng/mL} )</td>
<td>( \leq 60 \text{ ng/mL} )</td>
<td>Modification of reagents to improve tolerance to elevated levels of biotin.</td>
</tr>
</tbody>
</table>

VI Standards/Guidance Documents Referenced:

Deciding When to Submit a 510(k) for a Change to an Existing Device: Guidance for Industry and Food and Drug Administration Staff

Refuse to Accept Policy for 510(k)s: Guidance for Industry and Food and Drug Administration Staff
VII Performance Characteristics (if/when applicable):

A Analytical Performance:

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.

1. Internal Precision:

The precision of the Elecsys Syphilis assay was evaluated in an internal study using seven human serum samples, the PreciControl 1 and PreciControl 2 controls, and one lot of reagent. Two replicates of each serum sample and control were tested two times per day for 21 days. Human serum samples were prepared to create a panel of two negative samples (COI < 1.0), one low positive samples (COI approximately = 1.0), and four positive samples (COI > 1.0). The mean COI value, Repeatability Standard Deviation (SD) and percent coefficient of variation (%CV) as well as Intermediate Precision SD and %CV were calculated for each group of samples. A summary of the results is shown below.

<table>
<thead>
<tr>
<th>Sample</th>
<th>Mean [COI]</th>
<th>SD [COI]</th>
<th>CV [%] (UCL* 95%)</th>
<th>SD [COI]</th>
<th>CV [%] (UCL* 95%)</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Human serum 1</td>
<td>0.125</td>
<td>0.00192</td>
<td>1.5 (1.9)</td>
<td>0.00210</td>
<td>1.7 (1.9)</td>
<td>84</td>
</tr>
<tr>
<td>Human serum 2</td>
<td>0.888</td>
<td>0.0175</td>
<td>2.0 (2.4)</td>
<td>0.0264</td>
<td>3.0 (3.5)</td>
<td>84</td>
</tr>
<tr>
<td>Human serum 3</td>
<td>1.09</td>
<td>0.0173</td>
<td>1.6 (1.9)</td>
<td>0.0260</td>
<td>2.4 (2.9)</td>
<td>84</td>
</tr>
<tr>
<td>Human serum 4</td>
<td>4.11</td>
<td>0.0983</td>
<td>2.4 (2.9)</td>
<td>0.126</td>
<td>3.1 (3.6)</td>
<td>84</td>
</tr>
<tr>
<td>Human serum 5</td>
<td>6.88</td>
<td>0.198</td>
<td>2.9 (3.5)</td>
<td>0.249</td>
<td>3.6 (4.3)</td>
<td>84</td>
</tr>
<tr>
<td>Human serum 6</td>
<td>15.8</td>
<td>0.395</td>
<td>2.5 (3.0)</td>
<td>0.574</td>
<td>3.6 (4.3)</td>
<td>84</td>
</tr>
<tr>
<td>Human serum 7</td>
<td>16.4</td>
<td>0.395</td>
<td>2.4 (2.9)</td>
<td>0.540</td>
<td>3.3 (3.9)</td>
<td>84</td>
</tr>
<tr>
<td>PreciControl 1</td>
<td>0.0951</td>
<td>0.00107</td>
<td>1.1 (1.4)</td>
<td>0.00130</td>
<td>1.4 (1.6)</td>
<td>84</td>
</tr>
<tr>
<td>PreciControl 2</td>
<td>5.90</td>
<td>0.126</td>
<td>2.1 (2.6)</td>
<td>0.155</td>
<td>2.6 (3.0)</td>
<td>84</td>
</tr>
</tbody>
</table>

*Upper Confidence Limit

Multi-site Reproducibility:

See K160910

2. Linearity:

Not applicable; this is a qualitative assay.

3. Analytical Specificity/Interference:

Potential interference with specimens containing biotin was evaluated by testing three anti-\( T. pallidum \) antibody concentrations (negative, near cut-off and positive). 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.
The results of the study support the following statement in the assay labeling:

*Specimens that contain biotin at a concentration of 1200 ng/mL demonstrate less than or equal to 10 % negative bias in COI values.*

For complete endogenous substances interference study results see K160910.

4. **Assay Reportable Range:**
   See K160910

5. **Traceability, Stability, Expected Values (Controls, Calibrators, or Methods):**
   The claimed on-board reagent stability and calibration frequency reported in K160910 was confirmed with new studies.

6. **Detection Limit:**
   See K160910

7. **Assay Cut-Off:**
   See K160910

**B Comparison Studies:**

1. **Method Comparison with Predicate Device:**
   A method comparison study was conducted to confirm the modified assay yields equivalent performance compared to the unmodified assay. The results obtained from 232 samples distributed across the span of the reportable range were measured internally with one reagent lot of the current assay and three different reagent lots of the updated assay in single determination. The study showed 100% agreement of the qualitative results and regression analysis of the COI values demonstrated acceptable concordance between the assays. The results of the original method comparison study are found in K160910.

2. **Matrix Comparison:**
   See K160910

**C Clinical Studies:**

1. **Clinical Sensitivity:**
   See K160910

2. **Clinical Specificity:**
   See K160910

3. **Other Clinical Supportive Data (When 1. and 2. Are Not Applicable):**
   See K160910
D  Clinical Cut-Off:
   Not applicable

E  Expected Values/Reference Range:
   See K160910

VIII  Proposed Labeling:
   The labeling supports the finding of substantial equivalence for this device.

IX  Conclusion:
   The submitted information in this premarket notification is complete and supports a substantial equivalence decision.