August 18, 2021

Roche Diagnostics
Adennis Cora
Regulatory Affairs Consultant
9115 Hague Road
PO Box 50416
Indianapolis, IN 46250

Re: K203227
Trade/Device Name: Elecsys HCG STAT
Regulation Number: 21 CFR 862.1155
Regulation Name: Human chorionic gonadotropin (HCG) test system
Regulatory Class: Class II
Product Code: DHA
Dated: October 31, 2020
Received: November 2, 2020

Dear Adennis Cora:

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,

Marianela Perez- Torres, Ph.D.
Deputy Director
Division of Chemistry and Toxicology 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)*
K203227

Device Name

Elecsys HCG STAT

Indications for Use *(Describe)*

For the in vitro quantitative determination of human chorionic gonadotropin (hCG) in human serum and plasma. The Elecsys HCG STAT immunoassay is intended for use in the early detection of pregnancy.
The electrochemiluminescence immunoassay "ECLIA" is intended for use on the cobas e 601 immunoassay 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.

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Elecsys HCG STAT
K203227 Summary

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

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 Traditional 510(k) Premarket Notification is to obtain FDA review and clearance for the Elecsys HCG STAT on the **cobas e** 601.

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Date Prepared	March 17, 2021
Proprietary Name	Elecsys HCG STAT
Common Name	Beta HCG STAT Test
Classification Name	System, Test, Human Chorionic Gonadotropin
Product Codes, Regulation Numbers	DHA 21 CFR 862.1155
Predicate Devices	Elecsys HCG STAT (K002148)
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 HCG STAT immunoassay makes use of a sandwich test principle using monoclonal antibodies specifically directed against Human Chorionic Gonadotropin (HCG). The antibodies labeled with ruthenium complex consist of a chimeric construct from human and mouse specific components. The Elecsys HCG STAT immunoassay is used for the in vitro quantitative determination of human chorionic gonadotropin (hCG) in human serum and plasma. It is intended for use on the **cobas e** 601immunoassay analyzer.

2. INDICATIONS FOR USE

For the in vitro quantitative determination of human chorionic gonadotropin (hCG) in human serum and plasma. The Elecsys HCG STAT immunoassay is intended for use in the early detection of pregnancy.

The electrochemiluminescence immunoassay "ECLIA" is intended for use on the **cobas e** 601 immunoassay analyzer.

3. TECHNOLOGICAL CHARACTERISTICS

The reagent working solutions include:

Rack Pack (kit placed on the analyzer).

- M Streptavidin-coated microparticles (transparent cap), 1 bottle, 6.5 mL: Streptavidin-coated microparticles 0.72 mg/mL; preservative.
- R1 Anti-hCG-Ab~biotin (gray cap), 1 bottle, 9 mL: Biotinylated monoclonal anti-hCG antibody (mouse) 2.3 mg/L; phosphate buffer 40 mmol/L, pH 7.5; preservative.
- R2 Anti-hCG-Ab~Ru(bpy)$_3^{2+}$ (black cap), 1 bottle, 10 mL:Monoclonal anti-hCG antibody (mouse) labeled with ruthenium complex 6.0 mg/L; phosphate buffer 40 mmol/L, pH 6.5; preservative.

The following table compares the updated Elecsys HCG STAT with its predicate device, the current Elecsys HCG STAT (K002148).

Table 1: Technical Characteristics Comparison Table between updated Elecsys HCG STAT and current Elecsys HCG STAT

Feature	Candidate Device Updated Elecsys HCG STAT	Predicate Device Elecsys HCG STAT (K002148)
Intended Use	For the in vitro quantitative determination of human chorionic gonadotropin (hCG) in human serum and plasma. The Elecsys HCG STAT immunoassay is intended for use in the early detection of pregnancy. The electrochemiluminescence immunoassay "ECLIA" is intended for use on the **cobas e** 601 immunoassay analyzer.	Same
Assay Method	Sandwich Principle	Same
Detection Method	Electrochemiluminescence	Same
Applications/Test Time	9 minutes	Same
Instrument Platform	**cobas e** 601	**cobas e** 411, **cobas e** 601, **cobas e** 602, and **cobas e** 801
Sample Type/Matrix	Human serum, plasma	Same
Sample Anticoagulants	Li-heparin, K2-EDTA and K3-EDTA plasma.	Same
Calibrator	HCG STAT CalSet	Same
Calibration Method	Traceability: This method has been standardized against the 4th International Standard for Chorionic Gonadotropin from the National Institute for Biological Standards and Control (NIBSC) code 75/589. Every Elecsys reagent set has a barcoded label containing specific information for calibration of the particular reagent lot. The predefined master curve is adapted to the analyzer using the relevant CalSet.	Same

Feature	Candidate Device Updated Elecsys HCG STAT	Predicate Device Elecsys HCG STAT (K002148)
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). Calibration interval may be extended based on acceptable verification of calibration by the laboratory. 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)	Same
Controls	Controls for the various concentration ranges should be run individually at least once every 24 hours when the test is in use, once per reagent kit, and following each calibration. The control intervals and limits should be adapted to each laboratory's individual requirements. Values obtained should fall within the defined limits. Each laboratory should establish corrective measures to be taken if values fall outside the defined limits.	Same
Traceability/Standardization	This method has been standardized against the 4th International Standard for Chorionic Gonadotropin from the National Institute for Biological Standards and Control (NIBSC) code 75/589.	Same
Reagent Stability	**unopened** at 2-8 °C up to the stated expiration date **after opening** at 2-8 °C 12 weeks **on the analyzer** 4 weeks	Same
Measuring Range	1.0-10000 mIU/mL (defined by the Limit of Detection and the maximum of the master curve)	0.500-10000 mIU/mL (defined by the lower detection limit and the maximum of the master curve).

Feature	Candidate Device Updated Elecsys HCG STAT		Predicate Device Elecsys HCG STAT (K002148)	
Precision	Precision was evaluated on one cobas e 601 analyzer according to CLSI guideline EP05-A3. The protocol consisted of testing 5 Aliquots of each control (PreciControl Universal level 1 and PreciControl Universal level 2) and human serum samples (HS1-HS5) per run, 1 run per day for 5 days with 3 lots. Repeatability and intermediate precision (SD and CV values) were calculated according to CLSI EP05-A3. Precision was determined using Elecsys reagents, pooled human sera and controls in a protocol (EP05-A3) of the CLSI (Clinical and Laboratory Standards Institute): 2 runs per day in duplicate each for 21 days (n = 84).		Precision was determined using Elecsys reagents, pooled human sera and controls in a modified protocol (EP5-A) of the CLSI (Clinical and Laboratory Standards Institute): 6 times daily for 10 days (n = 60). Different Performance Data. Precision was determined using Elecsys reagents, pooled human sera and controls in a separate study according to protocol (EP5-A2) of the CLSI (Clinical and Laboratory Standards Institute): 2 runs per day in duplicate each for 21 days (n = 84).	
LoB	0.5 mlU/mL		Lower detection limit: 0.500 mIU/mL	
LoD	1.0 mIU/mL		Lower detection limit: 0.500 mIU/mL	
LoQ	1.0 mlU/mL		Lower detection limit: 0.500 mIU/mL	
Analytical Specificity	FSH 0.007 %, TSH 0.001 %		FSH 0.09 %, TSH: no cross-reactivity	
Biotin	This assay has no biotin interference in serum concentrations up to 1200 ng/mL.		≤ 164 nmol/L or ≤ 40 ng/mL	
Hook Effect	No Hook Effect up to ≥ 500,000 mIU/mL		Same	
Method Comparison	Updated Biotin assay (y) compared to current Elecsys HCG STAT assay (x)		Elecsys HCG STAT assay (y) with the Elecsys HCG+β assay (x)	
	Passing/Bablok y= 1.012x-0.970 T = 0.996	Linear regression y = 1.011x + 4.81 r = 1.000	Passing/Bablok y = 1.0x - 7.38 T = 0.986	Linear regression y = 1.05x - 5.26 r = 0.999

4. NON-CLINICAL PERFORMANCE EVALUATION

The non-clinical performance studies for the Elecsys HCG STAT are summarized below. The following performance data are provided in support of the substantial equivalence determination:

- Precision (5-Day and 21-Day) according to CLSI EP5-A3

- Detection Limit: LoB, LoD and LoQ according to CLSI EP17-A2
- Linearity according to CLSI EP6-A
- High Dose Hook Effect
- Interferences – Hemoglobin, Intralipid, Bilirubin, and Rheumatoid Factors
- Biotin Interference (CLSI EP07-A3)
- Common Drug Interferences
- Analytical Specificity/ Cross Reactivity (CLSI EP17-A2)
- Matrix Comparison - Anticoagulants
- Method Comparison to Predicate
- Reagent Stability (CLSI EP25-A)
- Lot Calibration Stability (CLSI EP25-A)

All performance specifications were met.

4.1. Precision

4.1.1. 21 Day Precision (1 lot on 3 sites)

Precision was evaluated on one **cobas e** 601 analyzer according to CLSI guideline EP05-A3. The protocol consisted of testing 2 replicates of each control (PreciControl Universal level 1 and PreciControl Universal level 2) and human serum samples (HS1-HS5) per run, 2 runs per day for 21 days with 1 lot. Repeatability and intermediate precision (SD and CV values) were calculated according to CLSI EP05-A3. Assay calibration was done as specified in the package insert.

4.1.2. 5 Day Precision

Precision was evaluated on one **cobas e** 601 analyzer according to CLSI guideline EP05-A3. The protocol consisted of testing 5 Aliquots of each control (PreciControl Universal level 1 and PreciControl Universal level 2) and human serum samples (HS1-HS5) per run, 1 run per day for

5 days with 3 lots. Repeatability and intermediate precision (SD and CV values) were calculated according to CLSI EP05-A3. Assay calibration was done as specified in the package insert.

4.1.3. Reproducibility

Reproducibility of the Elecsys HCG STAT assay was evaluated at three sites (1 internal and 2 external) on the **cobas e** 601 immunoassay analyzer using one lot of updated assay. The Reproducibility study was performed for a total of 1 run per day with 5 replicates of each human sera (HSP 1-6) and each control (CTR 1-2) per run, 1 run per day. The samples were run in randomized order on the analyzers. Human serum pools (HSP 1-4) and diluted single donor samples (HSP 5-6) were used to calculate Repeatability and Intermediate precision according to EP05-A3.

4.2. Analytical Sensitivity

4.2.1. Limit of Blank (LoB)

LoB of the Elecsys HCG STAT on the **cobas e** 601 analyzer was determined according to CLSI EP17-A2. Limit of Blank determines the highest observed measurement values for samples free of analyte. The Limit of Blank was determined as the 95th percentile of measurements of blank samples. For determination of LoB five analyte free samples were measured in two-fold determinations in 6 runs, distributed over ≥ 3 days, with 2 different lots on one **cobas e** 601 analyzer. In total 60 measured values of analyte free samples were obtained per lot. As the analyzers do not report negative sample concentrations the data set is truncated and the data were evaluated according to EP17-A2, chapter 5.3.3.1 as the linear interpolation of the 57th and 58th ranked observation.

4.2.2. Limit of Detection (LoD)

The 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. For determination of LoD five samples with low-analyte concentration (from LoB up to approx. 4 times the LoB) were measured in 2-fold determination in 6 runs, distributed over ≥ 3 days, with 2 different lots on one **cobas e** 601 analyzer. In total 60 measured values of samples with low

analyte concentrations were obtained per lot. Data analysis was based on determination of the 60 measured values of the 5 low analyte samples (according to CLSI EP17-A2, chapter 5.3.3.2).

4.2.3. Limit of Quantitation (LoQ)

For the determination of LoQ, 2 lots were evaluated, each with 5 human serum samples covering the range between LoB and 2x LoQ. Each sample was measured in 5 replicates (single determination of each replicate) with one run per day over 5 days on one **cobas e** 601 analyzer. Assay calibration was performed as specified in the package insert. Analyte-low samples or sample pools were used for the determination of LoQ.

The mean value and the intermediate precision as coefficient of variation (CV) and standard deviation (SD) were calculated for each LoQ sample. Data Analysis was determined according to CLSI EP17-A2.

4.3. Linearity/Assay Reportable Range

For linearity, one lot was tested on one **cobas e** 601 with one run. One human serum sample with high analyte content above the measuring range was diluted to the lower end of the measuring range with various amounts of human serum sample without analyte content. The dilution series contained 21 steps. Samples were assayed in 3-fold determinations. Data Analysis was determined according to CLSI EP6-A.

4.4. High Dose Hook Effect

The high-dose hook effect of the Elecsys HCG STAT assay was assessed with one reagent lot on one **cobas e** 601 analyzer in one-fold determination. Three human serum samples were spiked with analyte (HCG) to achieve high HCG concentrations. For each sample, a dilution series was performed using serum. The hook concentration reported corresponds to the highest analyte concentration that generates a signal ≥ 10% above the upper limit of the measuring range.

4.5. Endogenous Interferences

4.5.1. Hemoglobin/Intralipid/Bilirubin/Rheumatoid Factor

The effect on quantitation of analyte in the presence of endogenous interfering substances using the Elecsys HCG immunoassay was determined on one **cobas e** 601 analyzer for the following

four interfering substances: hemoglobin, intralipid, bilirubin and rheumatoid factor. The effect on quantitation of analyte in the presence of endogenous interfering substances was determined for HCG concentrations and a dilution set of the added interfering substances. For the sample with highest HCG concentration, spiked samples were used. One reagent lot was tested on 3 samples of each interfering substance.

One aliquot of each HCG sample (low, medium, high) was spiked with the interfering endogenous substance and used as "interference pool". Another aliquot of the sample was spiked with the same volume of the solvent of the interfering endogenous substance (without interfering substance) and used as the related "dilution pool". A series of at least 9 dilution steps were prepared by mixing the interference pools and the related dilution pools in 10 % increments.

The recovery (absolute deviation or % recovery) was calculated for each sample compared to the reference (unspiked) sample.

4.6. Biotin

The effect on quantitation of analyte in the presence of biotin using the Elecsys HCG STAT assay was determined on a **cobas e** 601 analyzer using three serum samples (low, medium, and high) concentration of HCG according to CLSI EP07-A3. One aliquot of each sample (low, medium, high) was spiked with biotin up to 3600 ng/mL and used as "interference pool". Another aliquot of the sample was spiked with the same volume of the solvent of the interfering endogenous substance (without interfering substance) and used as the related "dilution pool". A series of 11 dilution steps were prepared by mixing the interference pools and the related dilution pools. The recovery (absolute deviation or % recovery) were calculated for each sample compared to the reference (unspiked) sample. For the sample with highest HCG concentration, spiked samples were used.

4.7. Common drug Interferences

The effect on quantitation of analyte in the presence of drugs was determined by comparing values obtained from samples spiked with 17 common pharmaceutical compounds with the reference sample. One human serum sample was used and tested on the **cobas e** 601 immunoassay analyzer. Samples (with HCG concentrations near 5 mIU/mL

and near 50 mIU/mL) were divided into aliquots and spiked with the common drug interferents. The reference sample without drug was spiked with the respective amount of solvent.

4.8. Analytical Specificity/Cross-Reactivity

The analytical specificity of the Elecsys HCG STAT assay was determined with one reagent lot on one **cobas e** 601 analyzer using a human serum matrix with one HCG level (5 mIU/mL). The sample was spiked with the following potential cross-reactants: LH, FSH, and TSH. The sample was measured in presence and absence of the potential cross-reactants and cross reactivity was calculated using the following % Cross-reactivity formula:

$$= \frac{\text{mean analyte conc. of spiked sample} - \text{mean analyte conc. of unspiked sample}}{\text{spiked concentration of cross} - \text{reactant}} \text{ x } 100\%$$

4.9. Sample Matrix Comparison

The effect on quantitation of analyte in the presence of anticoagulants on the Elecsys HCG STAT assay. Values obtained from serum samples drawn into serum primary tubes (reference) were compared to Li-Heparin, K2-EDTA and K3-EDTA plasma. At least 40 serum/plasma pairs were tested in one run on one **cobas e** 601 analyzer. Data was assessed by Passing/Bablok regression analysis. Spiked samples were used when necessary for reaching high HCG concentrations but allotted for less than 10 % of all samples.

4.10. Method Comparison to Predicate

A method comparison (MC) study of the updated Elecsys HCG STAT assay (candidate device, Y) versus the predicate device, Elecsys HCG STAT current assay (X) was conducted on the **cobas e** 601 analyzer according to CLSI Guideline EP09-A3. Serum samples were measured internally using both the current and updated reagent formulations. One hundred thirty one (131) samples that span the measuring range were tested with 1 run per sample (no replicates). To sufficiently cover the measuring range, samples were spiked with recombinant HCG to cover the upper end of the measuring range, or diluted to cover the lower end of the measuring range.

Equivalence of the current Elecsys HCG STAT (K002148) assay and the updated Elecsys HCG STAT assay were evaluated as described below.

• Samples without further clinical or demographic information were used. Samples were distributed to span the reportable range.

• Calculation: Scatter-plot of numerical values of the current assay (x-axis) versus the updated assay (y-axis).

• Passing-Bablok analysis for slope and intercept was performed for the updated lot against the current lot.

4.11. 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.

4.12. Substantial Equivalence

The Elecsys HCG STAT immunoassay (updated assay, Mat. No. 08890587190) is substantially equivalent to the Elecsys HCG STAT immunoassay (current assay, Mat. No. 03300811190).