June 10, 2022

Roche Diagnostics
Edie Eads
US Regulatory Affairs Program Manager
9115 Hague Road
Indianapolis, Indiana 46250

Re: K203757
Trade/Device Name: Elecsys AMH
Regulation Number: 21 CFR 862.1092
Regulation Name: Anti-Mullerian Hormone Test System
Regulatory Class: Class II
Product Code: PQO
Dated: March 17, 2022
Received: March 21, 2022

Dear Edie Eads:

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
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)*
k203757

Device Name
Elecsys AMH

Indications for Use *(Describe)*
Elecsys AMH is intended for the in vitro quantitative determination of anti-Müllerian hormone (AMH) in human serum and lithium heparin plasma. The determination of AMH is used for the assessment of the ovarian reserve in women presenting to fertility clinics. This immunoassay is intended to distinguish between women presenting with AFC (antral follicle count) values > 15 (high ovarian reserve) and women with AFC values ≤ 15 (normal or diminished ovarian reserve). This immunoassay is intended to be used for assessing the ovarian reserve in conjunction with other clinical and laboratory findings before starting any fertility therapy. Elecsys AMH is not intended to be used for monitoring of women undergoing controlled ovarian stimulation in an Assisted Reproduction Technology program.

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.

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Elecsys AMH
510(k) Summary

This summary of 510(k) safety and effectiveness information is 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 AMH.

Submitter Name	Roche Diagnostics
Address	9115 Hague Road P.O. Box 50416 Indianapolis, IN 46250-0457
Contact	Contact: Edie Eads Phone: (317) 734-8046 Email: edie.eads@roche.com Secondary Contact: Todd Davis Phone: (317) 313-7112 Email: todd.davis@roche.com
Date Prepared	June 9, 2022
Proprietary Name	Elecsys AMH
Common Name	Elecsys AMH
Classification Name	Clinical Chemistry
Product Codes, Regulation Numbers	PQO, 21 CFR 862.1092
Predicate Devices	DEN150057, Elecsys AMH System

1. DEVICE DESCRIPTION

The Elecsys AMH immunoassay makes use of a sandwich test principle using a biotinylated monoclonal AMH-specific antibody and a monoclonal AMH-specific antibody labeled with a ruthenium complex. The Elecsys AMH immunoassay is intended for the quantitative determination of anti-Müllerian hormone (AMH) in human serum and lithium heparin plasma. It is intended for use on the **cobas e** immunoassay analyzers.

Results are determined via a calibration curve which is instrument-specifically generated by a two-point calibration and a master curve provided via the reagent barcode.

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-AMH-Ab~biotin (gray cap), 1 bottle, 8 mL: Biotinylated monoclonal anti-AMH antibody (mouse) 1.0 mg/L, phosphate buffer 50 mmol/L, pH 7.5; preservative.

- Anti-AMH-Ab~Ru(bpy) (black cap), 1 bottle, 8 mL: Monoclonal anti-AMH antibody (mouse) labeled with ruthenium complex 1.0 mg/L, biotin scavenger antibody 1 mg/mL, phosphate buffer 50 mmol/L, pH 7.5; preservative.

2. INTENDED USE/INDICATIONS FOR USE

Elecsys AMH is intended for the in vitro quantitative determination of anti-Müllerian hormone (AMH) in human serum and lithium heparin plasma. The determination of AMH is used for the assessment of the ovarian reserve in women presenting to fertility clinics. This immunoassay is intended to distinguish between women presenting with AFC (antral follicle count) values > 15 (high ovarian reserve) and women with AFC values ≤ 15 (normal or diminished ovarian reserve). This immunoassay is intended to be used for assessing the ovarian reserve in conjunction with other clinical and laboratory findings before starting any fertility therapy. Elecsys AMH is not intended to be used for monitoring of women undergoing controlled ovarian stimulation in an Assisted Reproduction Technology program.

The electrochemiluminescence immunoassay “ECLIA" is intended for use on **cobas e** immunoassay analyzers.

3. INDICATIONS FOR USE COMPARISON

The Elecsys AMH on the **cobas e** 601 (updated assay, Mat. No. 08819319160) is substantially equivalent to the Elecsys AMH system, granted under DEN150057.

The intended use was updated to remove additional components from the reagent intended use and to remove analyzers no longer supported for use with Roche assays. The indications for use was not changed for the Elecsys AMH from the predicate device.

Roche Diagnostics is updating the current Elecsys AMH to mitigate the potential interference of biotin. Roche implemented a technical solution consisting of a scavenger antibody to R2 allowing depletion of biotin in a patient sample by binding free biotin. There were no other technological changes to the current Elecsys AMH.

The submitted information in this premarket notification supports a substantial equivalence decision.

4. NON-CLINICAL AND/OR CLINICAL TESTS SUMMARY & CONCLUSIONS

Precision of the updated Elecsys AMH assay was evaluated with native human serum pools. The protocol consisted of testing two replicates per run, 2 runs per day for 21 days. Repeatability and Intermediate imprecision were calculated according to EP05-A3. All samples met the predetermined acceptance criteria.

Reproducibility was performed using a modified protocol, incorporating CLSI guidelines, Assay Migration Guidance, and the study performed in the original De Novo (DEN150057). Reproducibility was performed at three sites with three reagent lots for five days using native human serum pools. Overall reproducibility, repeatability (within run) and intermediate (within-lab) precision (SD and/or CV values) were calculated for the updated Elecsys AMH. Data calculation was performed according to CLSI EP05-A3. All sites met the specifications for

reproducibility testing. The results show that there is no influence of site variability on the performance of the assay.

The Limit of Blank (LoB) was determined according to CLSI EP17-A2. Five analyte-free samples were measured in two-fold determinations in six runs, distributed over 6 days using native human serum samples and serum pools. The LoB claim in the labeling will be set to 0.007 ng/mL.

The Limit of Detection (LoD) was determined according to CLSI EP17-A2. Five native samples with low-analyte concentration were measured in 2-fold determination in 6 runs, distributed over 6 days, on one analyzer. The LoB claim in the labeling will be set to 0.01 ng/mL.

The Limit of Quantitation (LoQ) was determined according to CLSI EP17-A2. Ten low-level human serum samples (HS) were measured in five-fold determinations with one run per day over 5 days. All lots met the predetermined acceptance criterion and the LoQ claim in the labeling will be set to 0.030 ng/mL.

Linearity was assessed using one human serum sample with high analyte content above the measuring range diluted to the lower end of the measuring range with postmenopausal female serum (pmpFS), which can be considered to contain no AMH. The dilution series contained 15 steps (dilutions) throughout the measuring range. Labeling will reflect, “Linearity results confirm the measuring range claim of 0.03 - 23 ng/mL for the Elecsys AMH assay.”

Accuracy and suitability of Diluent Universal for dilution of Elecsys AMH was assessed by diluting three high samples 1:2 with 2 different lots of Diluent Universal. The samples were manually diluted and multiplied by the dilution factor. Samples with AMH concentrations above the measuring range can be diluted with Diluent Universal 2 and the recommended dilution is 1:2 (either automatically by the analyzers or manually). The concentration of the diluted sample must be > 10 ng/mL.

The high-dose hook effect was assessed. Two high concentration samples were used to prepare a dilution series. For each sample, a dilution series was performed with postmenopausal female serum (pmpFS), which can be considered to contain no AMH. No hook effect up to ≥ 1400 ng/mL.

The effect of the presence of human anti-mouse antibodies (HAMA) was assessed in two-fold determination. A serum pool with a high-HAMA concentration and a serum pool without HAMA were each divided into three aliquots. Each set of three aliquots were spiked with different AMH concentrations. The serum pools spiked with AMH were diluted in 11 steps with the non-HAMA serum pool spiked with the same AMH concentration. The specification was fulfilled for the HAMA interference.

The effect on quantitation of AMH in the presence of biotin was tested with native human serum sample pools. Three human serum samples (containing low, mid, and high concentrations of AMH) were tested in duplicate with three reagent lots. The biotin interference claim will be set to 1200 ng/mL in labeling.

The effect on quantitation of AMH in the presence of seven endogenous interfering substances (Hemoglobin, Intralipid, Bilirubin, Rheumatoid Factor, Human IgG, Human IgM, and Human IgA) was tested using native human serum sample pools. For each potential interferent, three human serum samples (containing low, mid, and high concentrations of AMH) were tested in duplicate with one reagent lot. The results of endogenous interference testing met all specifications and there will be no changes from current AMH interference concentrations.

The specificity was determined using a native human serum pool without analyte content. The sample was spiked with potential cross-reactants. Samples were measured in the presence and absence of the potential cross-reactants and cross-reactivity was calculated with one lot of reagent.

Sixteen pharmaceutical compounds and four special pharmaceutical compounds were spiked into two human serum sample pools (low-AMH concentration and high-AMH concentration), and tested. The drug concentrations were chosen according to the recommendation (if available) given in the CLSI guideline EP07-A3. When concentrations were not available in the guideline, concentrations of at least three times of the maximum recommended daily dose were tested. All compounds met the acceptance criteria.

The effect on quantitation of AMH in the presence of lithium-heparin anticoagulant was determined by comparing values obtained from human samples drawn into Serum and Li-

Heparin plasma primary tubes. The specifications were fulfilled and thus the resulting data support the package-insert claim that Li-Heparin plasma is an acceptable sample type for use with the Elecsys AMH assay.

Roche performed method comparison studies in concordance with the "Assay Migration Studies for In Vitro Diagnostic Devices" guidance document and CLSI EP09-A3. Analyses were based on both quantitative and qualitative attributes of the assay. In total, all acceptance criteria were fulfilled for both quantitative and qualitative analyses; therefore, no clinically significant bias could be observed.

The stability studies were performed and the pre-specified acceptance criteria were met. The stability data supports the claims as reported in labeling.

The Elecsys AMH immunoassay (updated assay, Mat. No. 08819319160) is substantially equivalent to the Elecsys AMH system (current assay, Mat. No. 06331076160).