DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
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December 19, 2016

ROCHE DIAGNOSTICS
EDIE BRUNT
PRINCIPAL, US REGULATORY AFFAIRS
9115 HAGUE ROAD
INDIANAPOLIS, IN 46250

Re: DEN150057
Elecsys AMH system
Evaluation of Automatic Class III Designation – *De Novo* Request
Regulation Number: 21 CFR 862.1092
Regulation Name: Anti-mullerian hormone test system
Regulatory Classification: Class II
Product Code: PQO, JIT, JJX
Dated: December 11, 2015
Received: December 14, 2015

Dear Ms. Brunt:

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) has completed its review of your *de novo* request for classification of the Elecsys AMH system, a prescription device. The indications for use of the Elecsys AMH system is:

> Elecsys AMH system, consisting of the Elecsys AMH assay, AMH CalSet, PreciControl AMH, and AMH CalCheck 5, is intended for use in 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 ovarian reserve in women presenting to fertility clinics. This system 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 system is intended to be used for assessing the ovarian reserve in conjunction with other clinical and laboratory findings before starting any fertility therapy. The Elecsys AMH system is not intended to be used for monitoring of women undergoing controlled ovarian stimulation in an Assisted Reproduction Technology program.
>
> The Elecsys AMH system is intended for use on cobas e 411 analyzer.
>
> AMH CalSet is used for calibrating the quantitative Elecsys AMH assay.
>
> PreciControl AMH is used for quality control of the Elecsys AMH assay.

> AMH CalCheck 5 is an assayed control for use in calibration verification and for use in the verification of the assay range established for the Elecsys AMH assay.

FDA concludes that this device, and substantially equivalent devices of this generic type, should be classified into class II. This order, therefore, classifies the Elecsys AMH, and substantially equivalent devices of this generic type, into class II under the generic name "Anti-mullerian hormone test system."

FDA identifies this generic type of device as: Anti-mullerian hormone test system.

An anti-mullerian hormone test system is an in vitro diagnostic device intended to measure anti-mullerian hormone in human serum and plasma. An anti-mullerian hormone test system is intended to be used as an aid for assessing ovarian reserve in women.

Section 513(f)(2) of the Food, Drug and Cosmetic Act (the FD&C Act) was amended by section 607 of the Food and Drug Administration Safety and Innovation Act (FDASIA) on July 9, 2012. This new law provides two options for *de novo* classification. First, any person who receives a "not substantially equivalent" (NSE) determination in response to a 510(k) for a device that has not been previously classified under the Act may, within 30 days of receiving notice of the NSE determination, request FDA to make a risk-based classification of the device under section 513(a)(1) of the Act. Alternatively, any person who determines that there is no legally marketed device upon which to base a determination of substantial equivalence may request FDA to make a risk-based classification of the device under section 513(a)(1) of the Act without first submitting a 510(k). FDA shall, within 120 days of receiving such a request, classify the device. This classification shall be the initial classification of the device. Within 30 days after the issuance of an order classifying the device, FDA must publish a notice in the **Federal Register** classifying the device type.

On December 14, 2015, FDA received your *de novo* requesting classification of the Elecsys AMH system into class II. The request was submitted under section 513(f)(2) of the FD&C Act. In order to classify the Elecsys AMH into class I or II, it is necessary that the proposed class have sufficient regulatory controls to provide reasonable assurance of the safety and effectiveness of the device for its intended use.

After review of the information submitted in the *de novo* request, FDA has determined that the Elecsys AMH indicated for use as follows

> Elecsys AMH system, consisting of the Elecsys AMH assay, AMH CalSet, PreciControl AMH, and AMH CalCheck 5, is intended for use in 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 ovarian reserve in women presenting to fertility clinics. This system 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 system is intended to be used for assessing the ovarian reserve in conjunction with other clinical and laboratory findings before starting any fertility therapy. The Elecsys AMH system is

not intended to be used for monitoring of women undergoing controlled ovarian stimulation in an Assisted Reproduction Technology program.

The Elecsys AMH system is intended for use on cobas e 411 analyzer.

AMH CalSet is used for calibrating the quantitative Elecsys AMH assay.

PreciControl AMH is used for quality control of the Elecsys AMH assay.

AMH CalCheck 5 is an assayed control for use in calibration verification and for use in the verification of the assay range established for the Elecsys AMH assay.

can be classified in class II with the establishment of special controls for this type of device. FDA believes that class II special controls identified later in this order, along with the applicable general controls, including the design controls under 21 CFR part 820, provide reasonable assurance of the safety and effectiveness of the device type.

Table 1 – Identified Risks to Health and Identified Mitigations

Identified Risks to Health	Identified Mitigations
Inaccurate test results that provide false positive results may lead to a modification, delay or cancellation before a controlled ovarian stimulation procedure is initiated.	General controls and special controls (1) and (2)
Inaccurate test results that provide false negative results that may lead to the development of ovarian hyperstimulation syndrome in patients incorrectly thought to have normal and/or diminished ovarian reserve.	General controls and special controls (1) and (2)

In combination with the general controls of the FD&C Act, an anti-mullerian hormone test system is subject to the following special controls:

1) Premarket notification submissions must include the following information:
    i. An adequate traceability plan to minimize the risk of drift in anti-mullerian hormone test system results over time.
    ii. Detailed documentation of a prospective clinical study to demonstrate clinical performance or, if appropriate, results from an equivalent sample set. This detailed documentation must include the following information:
        a. Results must demonstrate adequate clinical performance relative to a well-accepted comparator.
        b. Clinical sample results must demonstrate consistency of device output throughout the device measuring range that is appropriate for the intended use population.
        c. Clinical study documentation must include the original study protocol (including predefined statistical analysis plan), study report documenting support for the proposed indications for use(s), and results of all statistical analyses.

iii. Reference intervals generated by testing an adequate number of samples from apparently healthy normal individuals in the intended use population.

2) Your 809.10(b) compliant labeling must include a warning statement that the device is intended to be used for assessing the ovarian reserve in conjunction with other clinical and laboratory findings before starting any fertility therapy, and that the device should be used in conjunction with the Antral Follicle Count.

In addition, this is a prescription device. Section 510(m) of the FD&C Act provides that FDA may exempt a class II device from the premarket notification requirements under section 510(k) of the FD&C Act, if FDA determines that premarket notification is not necessary to provide reasonable assurance of the safety and effectiveness of the device type. FDA has determined premarket notification is necessary to provide a reasonable assurance of safety and effectiveness of the device type, and therefore, the device is not exempt from the premarket notification requirements of the FD&C Act. Thus, persons who intend to market this device type must submit a premarket notification containing information on the Anti-Müllerian Hormone test system they intend to market prior to marketing the device and receive clearance to market from FDA.

Please be advised that FDA's decision to grant this *de novo* request does not mean that FDA has made a determination that your device complies with other requirements of the FD&C Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the FD&C 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 FD & C Act); 21 CFR 1000-1050.

A notice announcing this classification order will be published in the **Federal Register**. A copy of this order and supporting documentation are on file in the Dockets Management Branch (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Room 1061, Rockville, MD 20852 and are available for inspection between 9 a.m. and 4 p.m., Monday through Friday.

As a result of this order, you may immediately market your device as described in the *de novo* request, subject to the general control provisions of the FD&C Act and the special controls identified in this order.

If you have any questions concerning this classification order, please contact Lili Duan at 301-796-7404.

Sincerely,

Courtney H. Lias -S

Courtney H. Lias, Ph.D.
Director
Division of Chemistry and Toxicology
Devices
Office of In Vitro Diagnostics
and Radiological Health
Center for Devices and Radiological Health