November 13, 2017

Beckman Coulter, Inc.
Debbie Kidder
Senior Staff, Regulatory Affairs
1000 Lake Hazeltine Drive
Chaska, MN 55318-1084

Re: K170524
Trade/Device Name: Access AMH
Regulation Number: 21 CFR 862.1092
Regulation Name: Anti-Mullerian hormone test system
Regulatory Class: Class II
Product Code: PQO
Dated: October 5, 2017
Received: October 6, 2017

Dear Debbie Kidder:

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. 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); 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 Act); 21 CFR 1000-1050.

Silver Spring, MD 20993
www.fda.gov

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 http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/) and CDRH Learn (http://www.fda.gov/Training/CDRHLearn). 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 (http://www.fda.gov/DICE) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

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

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: 06/30/2020
See PRA Statement below.

510(k) Number *(if known)*
K170524

Device Name
Access AMH

Indications for Use *(Describe)*
The Access AMH assay is a paramagnetic particle chemiluminescent immunoassay for the quantitative determination of anti-Müllerian hormone (AMH) levels in human serum and lithium heparin plasma using the Access Immunoassay Systems as an aid in 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). The Access AMH is intended to be used in conjunction with other clinical and laboratory findings such as antral follicle count, before starting fertility therapy. The Access AMH is not intended to be used for monitoring of women undergoing controlled ovarian stimulation in an Assisted Reproduction Technology program.

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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510(k) Summary k170524
Date Prepared: November 9, 2017

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

Submitter's Name and Address

Beckman Coulter, Inc.
1000 Lake Hazeltine Drive
Chaska, MN 55318

Primary Contact: Debbie Kidder
(612)475-6022
(952) 368-7610 (fax)

Alternate Contact: Angela Kilian
(952) 368-1330
(952) 368-7610 (fax)

Device Name

Proprietary / Trade Name:	Access AMH
Common Name:	Anti-Müllerian hormone test system
Classification Name:	Anti-Müllerian hormone test system
Product Code PQO	(21 CFR 862.1092)

Predicate Device

Roche Elecsys® AMH System (DEN150057)
Manufactured by Roche Diagnostics GmbH

System Description

The Access AMH assay, Access AMH Calibrators, Access AMH QC, along with the Access 2 Immunoassay System analyzer comprise the Access Immunoassay System for the quantitative determination of anti-Müllerian hormone (AMH) levels in human serum and plasma.

Intended Use

The Access AMH assay is a paramagnetic particle chemiluminescent immunoassay for the quantitative determination of anti-Müllerian hormone (AMH) levels in human serum and lithium heparin plasma using the Access Immunoassay Systems as an aid in 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). The Access AMH is intended to be used in conjunction with other clinical and laboratory findings such as antral follicle count, before starting fertility therapy. The Access AMH is not intended to be used for monitoring of women undergoing controlled ovarian stimulation in an Assisted Reproduction Technology program.

Table 1: Comparison of Technological Characteristics to the AMH Assay Predicate

Parameter	Access AMH Assay	Predicate Roche Elecsys® AMH
Indication for Use	The Access AMH assay is a paramagnetic particle chemiluminescent immunoassay for the quantitative determination of anti-Müllerian hormone (AMH) levels in human serum and lithium heparin plasma using the Access Immunoassay Systems as an aid in the assessment of ovarian reserve in women presenting to fertility clinics. This system is intended to distinguish between women with AFC (antral follicle count) values >15 (high ovarian reserve) and women with AFC values ≤15 (normal or diminished ovarian reserve). The Access AMH is intended to be used in conjunction with other clinical and laboratory findings such as antral follicle count, before starting any fertility therapy. The Access AMH 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 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 ovarian reserve in women presenting to fertility clinics. The Elecsys AMH system is intended for use on Cobas e 411 analyzer This system is intended to distinguish between women 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.
Analyte Measured	anti-Müllerian hormone (AMH)	anti-Müllerian hormone (AMH)
Sample Type	Serum or plasma	Serum or plasma
Technology	Sandwich immunoassay	Sandwich immunoassay
Format	Chemiluminescent	Electochemiluminescense
Method	Automated	Automated
Measuring Range	0.08 – 24 ng/mL (0.57– 171 pmol/L)	0.01 – 23 ng/mL (0.071 – 164.2 pmol/L)
Reagent Stability	Unopened at 2° to 10°C until stated expiration date.	Unopened at 2° to 8°C up to stated expiration date.

Limit of Blank (LoB): Access AMH was designed to have a Limit of Blank of ≤ 0.01 ng/mL (0.07 pmol/L). In one study, LoB testing determined the LoB for Access AMH to be 0.0040 ng/mL (0.029 pmol/L).

Limit of Detection (LoD): The Access AMH assay was designed to have a Limit of Detection (LOD) of ≤ 0.02 ng/mL (0.14 pmol/L). In one study, LoD testing determined the LoD for Access AMH to be 0.0098 ng/mL (0.07 pmol/L).

Imprecision: The AMH assay exhibits total imprecision of less than or equal to 10% CV for concentrations greater than or equal to 0.16 ng/mL, and total standard deviation (SD) ≤0.032 ng/mL at concentrations < 0.16 ng/mL.

Precision Summary of Access 2 - three lots combined

	AMH (ng/mL) n=240	Within-run		Between-run		Intra-study (Within Lab)		Inter-study		Total Imprecision	
Sample	Mean	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Sample 1	0.09	0.002	2.8	0.001	1.7	0.003	3.3	0.004	4.4	0.005	5.5
Sample 2	2.61	0.052	2.0	0.041	1.6	0.066	2.5	0.035	1.3	0.075	2.9
Sample 3	8.56	0.161	1.9	0.175	2.0	0.238	2.8	0.152	1.8	0.282	3.3
Sample 4	17.16	0.380	2.2	0.289	1.7	0.478	2.8	0.155	0.9	0.502	2.9

Reproducibility was evaluated at four sites. Six samples spanning the analytical measuring range and three quality control samples were tested. Samples were evaluated on four Access 2 instruments in four replicates with two runs per day for 10 days.

Reproducibility Summary of Access 2

	AMH (ng/mL) N=320	Within Run (Repeatability)		Within Day		Between Day		Between Site		Reproducibility (Total Imprecision)	
	Mean	SD	% CV	SD	% CV	SD	% CV	SD	% CV	SD	% CV
Sample 1	0.48	0.010	2.1	0.003	0.6	0*	NA	0.010	2.1	0.015	3.1
Sample 2	0.94	0.017	2.1	0.001	0.1	0.005	0.5	0.024	2.5	0.030	3.2
Sample 3	2.58	0.049	1.9	0.010	0.4	0.018	0.7	0.055	2.1	0.076	2.9
Sample 4	5.14	0.100	1.9	0.050	1.0	0*	NA	0.094	1.8	0.146	2.8
Sample 5	10.21	0.182	1.8	0.060	0.6	0.051	0.5	0.158	1.5	0.253	2.5
Sample 6	16.16	0.292	1.8	0.107	0.7	0*	NA	0.181	1.1	0.360	2.2
QC1	1.00	0.023	2.0	0.002	0.2	0.004	0.4	0.021	2.1	0.032	3.2
QC2	5.04	0.106	2.2	0.015	0.3	0.035	0.7	0.086	1.7	0.141	2.8
QC3	15.22	0.345	2.3	0.054	0.4	0.051	0.3	0.006	0.0	0.353	2.3

*Default value when estimated variance was negative.

High-dose Hook Effect: The Access AMH assay demonstrated no high-dose hook effect up to 1,000 ng/mL in normal human serum spiked with recombinant AMH.

Dilution Recovery: The Access AMH assay has been demonstrated to dilute recover across the range of the assay (0 to 24 ng/mL) in plasma and serum samples. Samples containing AMH concentrations from approximately
0 – 24 ng/mL can be diluted 10-fold with an average recovery of 100 ± 10%.

Limit of Quantitation (LoQ): The Access AMH assay was designed to have a Limit of Quantitation (LOQ) of ≤ 0.08 ng/mL (0.57 pmol/L). In one study, the LoQ for Access AMH was determined to be 0.013 ng/mL (0.093 pmol/L).

Linearity: The Access AMH was designed to be linear, with a maximum deviation from linearity of ≤ 5% for samples > 0.16 ng/mL, and ≤ 0.04 ng/mL for samples ≤ 0.16 ng/mL. One study analyzed using a polynominal regression method demonstrated a maximum deviation from linearity of 4.8% for samples > 0.16 ng/mL and <0.00 ng/mL for samples ≤0.16 ng/mL.

Linearity – Expected and Observed Concentrations

	Reagent Lot 470103 Calibrator Lot P2 Access 2 #504310		**Reagent Lot 470116 Calibrator Lot P3 Access 2 #504310**		**Reagent Lot 470103 Calibrator Lot P2 Access 2 #506902**		**Reagent Lot 470116 Calibrator Lot P2 Access 2 #506902**		**Reagent Lot 470098 Calibrator Lot P1 Access 2 #501022**		**Reagent Lot 470098 Calibrator Lot P2 Access 2 #509403**	
Sample	**Expected Result (ng/mL)**	**Observed Result (ng/mL)**	**Expected Result (ng/mL)**	**Observed Result (ng/mL)**	**Expected Result (ng/mL)**	**Observed Result (ng/mL)**	**Expected Result (ng/mL)**	**Observed Result (ng/mL)**	**Expected Result (ng/mL)**	**Observed Result (ng/mL)**	**Expected Result (ng/mL)**	**Observed Result (ng/mL)**
Sample 1	0.00	0.00	0.00	0.0025	0.00	0.00	0.01	0.005	0.004	0.004	0.004	0.004
Sample 2	3.22	3.14	3.26	3.17	2.88	3.08	2.87	3.1	3.02	2.91	3.04	2.93
Sample 3	6.44	6.18	6.51	6.10	5.76	5.82	5.73	5.86	6.04	5.97	6.08	5.93
Sample 4	9.66	9.17	9.76	9.02	8.64	8.99	8.59	9.15	9.06	8.74	9.12	8.80
Sample 5	12.88	12.57	13.02	12.29	11.52	11.86	11.45	11.87	12.08	11.54	12.17	11.92
Sample 6	16.10	15.28	16.27	15.29	14.10	14.23	14.32	14.36	15.10	14.74	15.21	14.79
Sample 7	19.32	18.45	19.52	18.79	17.28	17.39	17.18	17.67	18.12	17.94	18.26	19.30
Sample 8	22.54	21.71	22.77	22.14	20.16	20.81	20.04	20.61	21.14	21.36	21.29	21.22
Sample 9	25.75	25.76	26.03	26.03	23.04	23.30	22.90	22.90	24.16	23.80	24.33	24.46

Analytical Specificity:

Serum samples with AMH concentrations of approximately 2 and 10 ng/mL (14.3 and 71 pmol/L) were spiked with concentrations of the substances below and run on a single Access 2 Immunoassay System. Total Protein (human serum albumin) was tested in serum samples with AMH concentrations of approximately 2 and 7 ng/mL (14.3 and 50 pmol/L). Values were calculated as described in CLSI EP7-A2. Interference was determined by testing controls (no interfering substance added) and matched test samples (with interfering substance added). There was no significant interference (exceeding 10% shift in dose) observed when the following substances were tested at the indicated concentrations.

Substance	Highest Concentration Added
Acetaminophen	20 mg/dL
Acetylsalicylic acid	65 mg/dL
Ampicillin sodium salt	1000 mg/L
Ascorbic acid	170 µmol/L
Bilirubin (Conjugated)	43 mg/dL
Bilirubin (Unconjugated)	40 mg/dL
Biotin	179 ng/mL
Cefoxitin sodium salt	2500mg/L
Cyclosporin A	5 mg/L
Doxycycline hyclate	50 mg/L
Folic acid	0.4 mg/L
Gamma Globulin	60 mg/L
Hemoglobin	1 g/dL
Heparin (low molecular weight)	3000 U/L
Ibuprofen	50 mg/dL
IgA	1.8 g/dL
IgG	2.5 g/dL
IgM	0.5 g/dL
Intralipids	37 mmol/L
Levodopa	20 mg/L

Levothyroxine sodium hydrate	0.2 mg/L
Metformin	2000 mg/L
Methyldopa	20 mg/L
Metronidazole	200 mg/L
N-Acetyl-L-cysteine	150 mg/L
Phenylbutazone	400 mg/L
Rheumatoid Factor	1000 IU/mL
Rifampicin	60 mg/L
Theophylline	100 mg/L
Triptoréline (Gonapeptyl)	0.1 mg/L
Total protein (human serum albumin)	12 g/dL
Uric Acid	1.4 mmol/L

Cross-reactivity:

Serum samples with AMH concentrations of approximately 2 and 10 ng/mL (14.3 and 71 pmol/L) spiked with concentrations of the substances below and run on a single Access 2 Immunoassay System. Activin A was tested in serum samples with AMH concentrations of approximately 1 and 5 ng/mL (7.1 and 36 pmol/L). Values were calculated per CLSI EP7-A2. There was no significant cross reactivity (exceeding 5% cross reactivity) observed when the following substances were tested at the indicated concentrations:

Cross-reactant Substance	**Highest Concentration Added**
Inhibin A	100 ng/mL
Activin A	16.32 µg/L
hLH	100 mIU/mL
hFSH	115 mIU/mL
TGF ß-1	65 ng/mL

Matrix Comparison: A comparison of fifty-seven (57) matched sets of serum (gel and no gel) and plasma (lithium-heparin) samples with AMH concentrations spanning as much of the assay range as practicably possible. All sample type combinations pass the specification of slope equal to 1.00 ± 0.10.

Sample type comparison	Slope	Sample Range (ng/mL)	N
Lithium Heparin vs.Serum No Gel	1.03	0.20 to 13.75	57
Lithium Heparin vs. Serum Gel	1.05	0.19 to 13.71	57
Serum Gel vs. Serum No Gel	0.99	0.20 to 13.75	57

Method Comparison: A comparison of 121 values across the range of the assay using the Access AMH assay on the Access 2 Immunoassay system and a commercially available immunoassay kit gave the following statistical data using Passing Bablok regression and Spearman correlation for the r calculation:

N	Range of Observations (ng/mL)	Intercept (ng/mL)	Slope (95% CI)	Correlation Coefficient (r)
121	0.070 to 22.80	0.04	1.03 (1.01 – 1.06)	0.99

Access AMH Clinical Study: A multicenter, clinical study of 164 women was used to correlate AMH values to the antral follicle count (AFC) in women presenting to fertility clinics for evaluation. The trial enrolled women at 13 geographically diverse sites in the US who were between ≥ 21 and < 46 years of age (mean age 34.9 years, range of 23 to 45 years). The women were in their first cycle of ovarian stimulation for IVF or IVF/ICSI, with both ovaries present and a regular menstrual cycle, and without confirmed polycystic ovary syndrome (PCOS). The mean body mass index (BMI) of all participating women averaged 25.1 with a standard deviation of ± 5.3. The AFC result was determined by transvaginal ultrasonography, which measured follicles of 2 to 10 mm in diameter. The AFC and AMH were determined on days 2 - 4 of the same spontaneous menstrual cycle. The trial demonstrated that the AMH levels measured for these subjects (N) correlate well with the AFC results ($r = 0.77$, $p < 0.0001$).

The AFC results were sorted into 2 groups: ≤ 15 (67%) or > 15 (33%). For the > 15 AFC group the AMH cutoff is 1.77 ng/mL. The corresponding sensitivity and specificity were 88.9% and 59.1%, respectively.
For patients with an AMH concentration that was > 1.77 ng/mL, 52% were in the > 15 AFC group and 48% were in the ≤ 15 AFC group. The study results support the system can distinguish between women with AFC values > 15 (high ovarian reserve) and women with AFC values ≤ 15 (normal or diminished ovarian reserve).

Expected Reference Intervals: The serum and plasma samples were prospectively procured from apparently healthy, non-pregnant females at five (5) geographically diverse sites. Subjects were required to have regular menstrual cycles between 21 and 35 days, both ovaries present, and proven fertility. Populations studied are described by group in the table below.

Serum AMH			
Group (years)	**Sample Size**	**Median ng/mL (pmol/L)**	**95% Reference Interval ng/mL (pmol/L)**
18-25	120	3.6 (25.70)	**1.02 – 14.63 (7.28 - 104.46)**
26-30	131	3.82 (27.27)	**0.69 – 13.39 (4.93 - 95.60)**
31-35	120	2.47 (17.64)	**0.36 - 10.07 (2.57 - 71.90)**
36-40	123	1.71 (12.21)	**0.18 - 5.68 (1.29 - 40.56)**
41-45	126	0.54 (3.86)	**0.01 – 2.99 (0.07 - 21.35)**

Plasma AMH			
Group (years)	**Sample Size**	**Median ng/mL (pmol/L)**	**95% Reference Interval ng/mL (pmol/L)**
18-25	120	3.75 (26.78)	**1.04 – 15.25 (7.43 - 108.89)**
26-30	131	4.06 (28.99)	**0.74 – 13.81 (5.28 - 98.60)**
31-35	120	2.56 (18.28)	**0.38 - 10.50 (2.71 - 74.97)**
36-40	123	1.78 (12.71)	**0.19 – 6.06 (1.36 - 43.27)**
41-45	126	0.56 (4.00)	**0.01 – 3.17 (0.07 - 22.63)**

Conclusion:

The conclusions drawn from the nonclinical and clinical testing demonstrate that the Access AMH assay for use on the Access Immunoassay Systems, are as safe, as effective, and performs as well as the predicate.