510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY

I Background Information:

A 510(k) Number

K223679

B Applicant

Beckman Coulter Inc

C Proprietary and Established Names

Access AMH

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
PQO	Class II	21 CFR 862.1092 - Anti-Mullerian Hormone Test System	CH - Clinical Chemistry

II Submission/Device Overview:

A Purpose for Submission:

Modification to a previously cleared device

B Measurand:

Anti-Müllerian hormone (AMH)

C Type of Test:

Quantitative chemiluminescent immunoassay

III Intended Use/Indications for Use:

A Intended Use(s):

See Indications for Use below.

B Indication(s) 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 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.

C Special Conditions for Use Statement(s):

- Rx - For Prescription Use Only
- Samples for AMH levels should be drawn on days 2- 4 of the menstrual cycle.
- The Access AMH assay is intended to be used for assessing the ovarian reserve in conjunction with other clinical and laboratory findings before starting any fertility therapy (including pre-treatment such GnRH agonist down-regulation therapy) and should be used in conjunction with AFC.
- The Access AMH assay is not intended to be used for monitoring of women undergoing controlled ovarian stimulation in an Assisted Reproduction Technology program.

D Special Instrument Requirements:

Performance data shown below was collected on the DxI 9000 Access Immunoassay analyzer.

IV Device/System Characteristics:

A Device Description:

The Access AMH assay reagent pack consists of the following components:

- R1a: Paramagnetic particles coated with mouse monoclonal anti-AMH in TRIS buffer with surfactant, protein (bovine), <0.1% sodium azide, 0.1% ProClin 300
- R1b: Mouse anti-AMH alkaline phosphatase conjugate in MES buffer, surfactant, protein (bovine, recombinant), <0.1% sodium azide, 0.1% ProClin 300

- R1c: TRIS buffer with surfactant, protein (murine, bovine), <0.1% sodium azide, 0.1% ProClin 300

B Principle of Operation:

The Access AMH assay is a simultaneous one-step immunoenzymatic ("sandwich") assay. A sample is added to a reaction vessel, along with a mouse monoclonal anti-AMH antibody conjugated to alkaline phosphatase in MES buffer, TRIS buffered saline with proteins, and paramagnetic particles coated with a mouse monoclonal anti-AMH antibody in TRIS buffer.

After incubation in a reaction vessel, materials bound to the solid phase are held in a magnetic field while unbound materials are washed away. Then, the chemiluminescent substrate is added to the vessel and light generated by this reaction is measured with a luminometer. The light production is directly proportional to the concentration of AMH in the sample. The amount of analyte in the sample is determined from a stored, multi-point calibration curve.

V Substantial Equivalence Information:

A Predicate Device Name(s):

Access AMH

B Predicate 510(k) Number(s):

K170524

C Comparison with Predicate(s):

Device & Predicate Device(s):	K223679	K170524
Device Trade Name	Access AMH	Access AMH
General Device Characteristic Similarities		
Intended Use/Indications For Use	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	Same

	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.	
Analyte	Anti-Müllerian hormone (AMH)	Same
Sample Type	Serum and lithium heparin plasma	Same
Measuring Range	0.08-24 ng/mL	Same
General Device Characteristic Differences		
Substrate	Lumi-Phos PRO Substrate	Access Substrate
Instrument	DxI 9000 Access Immunoassay analyzer	Access 2 Immunoassay system

VI Standards/Guidance Documents Referenced:

- CLSI EP17- A2, Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline – Second Edition.
- CLSI EP05-A3, Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline-Third Edition.
- CLSI EP06-Ed2, Evaluation of the Linearity of Quantitative Measurement Procedures; Approved Guideline.
- CLSI EP09c-A3, Method Procedure Comparison and Bias Estimation Using Patient Samples; Approved Guideline – Third Edition.

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility:

Precision studies were performed based on CLSI EP05-A3 to estimate repeatability and within-laboratory precision. The study was run on three DxI 9000 Immunoassay analyzers and three reagent pack lots. Six serum samples and 3 value assigned quality control samples spanning the claimed measuring range were used in the determination of imprecision. Each sample was assayed in duplicate with two runs per day, over 22 days for a total of 44 runs and 88 replicates per sample on each instrument and reagent lot combination. Each instrument was evaluated with one reagent lot. The within-run, between-run, between-day, and total imprecision was calculated. Results from multiple lots were similar. Results from one representative lot are provided in the table below:

AMH (ng/mL)			Repeatability (Within-Run)		Between-Run		Between-Day		Within-Laboratory	
Sample	**N**	**Mean**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**
Sample 1	88	0.29	0.010	3.6	0.006	2.0	0.006	2.0	0.013	4.6
Sample 2	88	0.80	0.030	3.7	0.000	0.0	0.000	0.0	0.030	3.7
QC Sample 1	88	1.0	0.03	3.0	0.02	2.1	0.03	3.0	0.05	4.8
Sample 3	88	2.4	0.11	4.5	0.00	0.0	0.05	2.0	0.12	5.0
QC Sample 2	88	5.1	0.18	3.4	0.03	0.7	0.09	1.7	0.20	3.9
Sample 4	88	6.9	0.19	2.8	0.00	0.0	0.16	2.3	0.25	3.6
Sample 5	88	13	0.4	3.1	0.3	1.9	0.3	2.6	0.6	4.5
QC Sample 3	88	16	0.7	4.4	0.0	0.0	0.5	3.1	0.8	5.4
Sample 6	88	19	0.5	2.6	0.3	1.8	0.3	1.4	0.6	3.4

A reproducibility study was conducted based on CLSI EP05-A3 to assess instrument-to-instrument variability. Seven serum samples with different AMH concentrations were run on three DxI 9000 Immunoassay analyzers. The samples were tested across three reagent lots and one calibrator lot on each instrument with five replicates per run and one run per day over five days. The within-run, between-day, between-instrument, and reproducibility was calculated for each reagent lot. Results from multiple lots were similar. Results from one representative lot are provided below:

Concentration (ng/mL)			Repeatability (Within-run)		Between-day		Between - instrument		Reproducibility	
Sample	**N**	**Mean**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**
Sample1	75	0.013	0.000	3.5	0.000	1.3	0.000	2.2	0.001	4.3
Sample2	75	0.28	0.008	2.8	0.003	1.0	0.002	0.7	0.009	3.1
Sample3	75	0.79	0.017	2.2	0.000	0.0	0.008	1.0	0.019	2.4
Sample4	75	2.4	0.09	3.7	0.02	1.0	0.00	0.0	0.09	3.8
Sample5	75	7.0	0.19	2.7	0.06	0.9	0.09	1.3	0.22	3.1
Sample6	75	13	0.3	2.3	0.2	1.7	0.2	1.7	0.4	3.3
Sample7	75	19	0.5	2.8	0.1	0.8	0.4	2.3	0.7	3.7

2. Linearity:

Linearity was evaluated based on CLSI EP06-Ed2. A native sample containing a concentration of AMH at the low end of the measuring interval was obtained. Two serum samples were mixed to create a sample at the high end of the measuring interval. In addition to the high and low AMH concentration samples, seven (7) mixtures were tested in this study. These samples were prepared independently by using incrementally larger proportions of the high sample diluted with the low sample, in order to achieve AMH concentrations that covered the range of the assay. The low sample was run in replicates of eight, and all other samples were run in replicates of four (4). This study was run on three DxI 9000 Immunoassay analyzers, using three reagent lots. The data was analyzed using a weighted linear regression model as described in the guideline. Results for a representative linear data fit are shown below:

$y = 0.9935x + 0.0001$

The results support the claimed measuring range of 0.08 to 24 ng/mL.

3. Analytical Specificity/Interference:

Potential cross-reactivity, interference, and high dose effect were evaluated in K170524. No cross reactivity, interference, or high dose effect was observed.

HAMA/Heterophile interference
HAMA/heterophile interference has not been evaluated for this device. The labeling contains the following limitation:

"For assays employing antibodies, the possibility exists for interference by heterophile antibodies in the patient sample. Patients who have been regularly exposed to animals or have received immunotherapy or diagnostic procedures utilizing immunoglobulins or immunoglobulin fragments may produce antibodies, e.g., HAMA, that interfere with immunoassays. Additionally, other heterophile antibodies such as human anti-goat antibodies may be present in patient samples. Such interfering antibodies may cause erroneous results. In rare cases, interference due to extremely high titers of antibodies to analyte-specific antibodies can occur. Carefully evaluate the applicability of this assay in patients suspected of having HAMA/heterophile antibodies."

4. Assay Reportable Range:

   The assay reportable range is 0.08 to 24 ng/mL.

5. Traceability, Stability, Expected Values (Controls, Calibrators, or Methods):

   The Access AMH assay traceability remains unchanged since the clearance of K170524. The assay is traceable to internal reference standards (primary reference calibrators), which consist of recombinant AMH in a BSA matrix. A detailed traceability plan was reviewed and found acceptable in K170524.

6. Detection Limit:

   The Limit of Blank, Limit of Detection, and Limit of Quantitation were determined in accordance with CLSI EP17-A2.

   Limit of Blank (LoB): The sponsor defined the Limit of Blank (LoB) as the non-parametric 95th percentile value from 75 measurements of five different blank samples obtained on three DxI 9000 Immunoassay analyzers with three reagent pack lots. The sponsor claims a LoB of 0.001 ng/mL.

   Limit of Detection (LoD): The maximum observed LoD is taken as the reported value for the measurement. The LoD estimate for the AMH assay is 0.002 ng/mL on the DxI 9000 Immunoassay analyzer.

   Limit of Quantitation (LoQ): To calculate the LoQ, three DxI 9000 Immunoassay analyzers were used with three reagent pack lots and three calibrator lots. Eleven native serum samples containing low levels of AMH analyte were prepared. Each of the samples were run in replicates of nine, in one run per day, for five days on three reagent pack lots (45 replicates of each sample on each reagent lot). The sponsor defined the LoQ as the lowest concentration of analyte that can be quantified with a total precision of ≤ 20% CV. The results provided demonstrate the 20% CV LoQ estimate for the Access AMH assay is 0.003 ng/mL. The claimed LoQ is 0.08 ng/mL.

7. Assay Cut-Off:

   To predict an antral follicle count of > 15, the corresponding AMH cutoff is 1.77 ng/mL.

B Comparison Studies:

1. Method Comparison with Predicate Device:

   A method comparison study was performed comparing the candidate Access AMH assay on the DxI 9000 Access Immunoassay analyzer to the comparator device, the predicate Access AMH assay run on the Access 2 Immunoassay system using a protocol based on CLSI EP09c-A3. A total of one hundred twenty-six (126) native serum samples were run on three DxI 9000 instruments and three Access 2 instruments with three reagent pack lots and three calibrator lots. Results analyzed using Passing-Bablok linear regression are shown below:

N	Slope	Intercept	Correlation Coefficient R
126	1.02 (1.00- 1.03)	0.011	1.00

2. Matrix Comparison:

A matrix comparison study was conducted in K170524 and demonstrates equivalent performance between serum and lithium heparin plasma.

C Clinical Studies:

1. Clinical Sensitivity:

Clinical sensitivity was established in K170524.

2. Clinical Specificity:

Clinical specificity was established in K170524.

3. Other Clinical Supportive Data (When 1. and 2. Are Not Applicable):

Not Applicable.

D Clinical Cut-Off:

The clinical cutoff validated in the clinical study is 1.77 ng/mL to distinguish women with an AFC >15 or ≤ 15. This cutoff is the same as for the predicate device.

E Expected Values/Reference Range:

The reference range information was established in K170524.

VIII Proposed Labeling:

The labeling is sufficient, and it satisfies the requirements of 21 CFR Parts 801 and 809, as applicable and the special controls for this device type under 21 CFR 862.1092.

IX Conclusion:

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