510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY

A. 510(k) Number:
k081754

B. Purpose for Submission:
New Device

C. Measurand:
Score based on 5 serum analytes

D. Type of Test:
Software algorithm and 5 immunoassays

E. Applicant:
Vermillion, Inc.

F. Proprietary and Established Names:
OVA1™ Test

G. Regulatory Information:

1. Regulation section:
   21 CFR 866.6050 Ovarian adnexal mass assessment score test system
2. Classification:
   Class II
3. Product code:
   ONX Serum, algorithm, ovarian cancer assessment test
4. Panel:
   Immunology (82)

H. Intended Use:

1. Intended use:
   The OVA1™ Test is a qualitative serum test that combines the results of five immunoassays into a single numerical score. It is indicated for women who meet the following criteria: over age 18; ovarian adnexal mass present for which surgery is planned, and not yet referred to an oncologist. The OVA1 Test is an aid to further assess the likelihood that malignancy is present when the physician's independent clinical and radiological evaluation does not indicate malignancy. The test is not intended as a screening or stand-alone diagnostic assay.

PRECAUTION: The OVA1™ Test should not be used without an independent clinical/radiological evaluation and is **not** intended to be a screening test or to determine whether a patient should proceed to surgery. Incorrect use of the OVA1™ Test carries the risk of unnecessary testing, surgery, and/or delayed diagnosis.

2. Indications for Use:
   Same as Intended Use.
3. Special conditions for use statement(s):
   Prescription Use only.
4. Special instrument requirements:
   The Siemens BN™ II System for the measurement of Prealbumin (also known as

Transythretin; TT), Apolipoprotein A-1 (Apo A-1), β_2-microglobulin (β_2M), and Transferrin (Tfr). The Roche Elecsys® 2010 for the measurement of CA 125. Both instrument systems are FDA cleared.

I. Device Description:

The OVA1™ Test uses OvaCalc Software to incorporate the values for 5 analytes from separately run immunoassays (described below) into a single numerical score between 0.0 and 10.0.

The cleared test system consists of the software, instruments, assays and reagents used to obtain the OVA1™ Test result. The immunoassays and reagents are sold separately from the OvaCalc Software. Users are instructed to use only those lots identified by Vermillion. The immunoassays are performed according to the manufacturers' directions detailed in each product insert. The analytes and corresponding tests and calibrators used in the OVA1™ Test are:

Analyte	Device (Assay and Calibrator)	Instrument
CA 125	Elecsys CA 125 II CA125 II CalSet	Roche Elecsys 2010
Prealbumin	N Antisera to Human Prealbumin and Retinal-binding Protein N Protein Standard SL (human)	Siemens BN II
Apolipoprotein A-1	N-Antisera to Human Apolipoprotein A-1 and Apolipoprotein B N Apolipoprotein Standard Serum (human)	Siemens BN II
β_2-microglobulin	Human Beta-2 Microglobulin Latex Enhanced Nephelometric Kit (Binding Site)	Siemens BN II
Transferrin	N Antisera to Human Transferrin and Haptoglobin N Protein Standard SL (human)	Siemens BN II

J. Substantial Equivalence Information:

1. Predicate device name(s):
   Not applicable
2. Predicate K number(s):
   Not applicable
3. Comparison with predicate:
   Not applicable

K. Standard/Guidance Document Referenced (if applicable):

ISO 14971:2007 Medical Devices-Application of Risk Management to Medical Devices, International Organization for Standardization, 2nd Edition.
CLSI guideline EP5-A2 "Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline."

L. Test Principle:

The individual assays for prealbumin, apolipoprotein A1 and transferrin each contain a biomarker specific rabbit polyclonal antibody which forms an immune complex with the target when reacted with a serum specimen. The immune complexes are

proportional to the concentration of biomarker in the serum specimen for each specific assay. The assay for β_2-microglobulin consists of polystyrene particles coated with a monospecific antiserum to β_2-microglobulin which aggregate when mixed with serum specimen β_2-microglobulin. These aggregates are proportional to the concentration of β_2-microglobulin in the serum specimen. The Siemens BN™ II System is an automated immunonephelometer.

The CA 125 II assay uses 2 mouse monoclonal antibodies to CA 125. The quantity of CA 125 present is then measured by chemiluminescence emission. The Roche Elecsys® 2010 is an automated analyzer with electrochemiluminescence detection. The amount of analyte in each assay is determined against the calibration curve. Each assay uses its own specific calibrator and controls.

The user enters results of the five analytes manually into an Excel spreadsheet together with the headers needed by OvaCalc Software. There is no physical or electronic connection between the immunoassay devices and the OvaCalc Software. Using an algorithm and the values of these 5 analytes, the OvaCalc Software generates a single unit-less numerical score from 0.0 to 10.0.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

   a. Precision: Precision performance of the OVA1™ Test was evaluated in accordance with CLSI guideline EP5-A2 "Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline." Five serum specimens spanning the OVA1™ Test score range (range of numerical results for OVA1™ Test: 0.0 to 10.0) were tested over 20 days, two runs per day, and two replicates per run. There were no unevaluable results. Total percent coefficient of variation (%CV) ranged from 1.0 to 7.4%.

Sample	n	OVA1 (Mean)	Within-run		Between-run		Total	
			SD	%CV	SD	%CV	SD	%CV
1	80	2.74	0.065	2.4	0.011	0.4	0.091	3.3
2	80	3.39	0.101	3.0	0.099	2.9	0.159	4.7
3	80	3.74	0.149	4.0	0.097	2.6	0.192	5.1
4	80	4.69	0.290	6.2	0.000	0.0	0.349	7.4
5	80	9.94	0.061	0.6	0.051	0.5	0.098	1.0

Lot-to-Lot precision: Five serum specimens and a minimum of two control sera from the same lot that yield two different OVA1™ Test scores (e.g., high and low, or low and near cutoff score) were analyzed at one site with three different reagent kit lots and calibrators over three different days by one operator. Reagents and calibrators were analyzed as shown:

Day	Calibrator	Reagent Lots		
1	1	A	B	C
2	2	B	C	B
3	3	C	A	A

Note: β2M calibrators and reagents are kit specific and are not interchangeable between kits. Therefore the three lots were analyzed on 3 separate days, and calibrators and reagents were not mixed between the lots (as shown) for this assay. For each of the five specimens and the two controls, the mean and standard deviation (SD) for the between-lot component of variance for each sample were calculated. The %CV for imprecision was ≤ 8.6% for any of the 5 samples.

Reproducibility: Five serum specimens spanning the OVA1™ Test score range and a minimum of two controls per day were tested in duplicate, two runs each day, over 6 days, by two operators at each of three sites. Each operator performed the test on three nonconsecutive days, i.e., operator 1 ran the test on days 1, 3, and 5; operator 2 ran the test on days 2, 4, and 6. At each site, the test was run with the same lots of calibrators, kit reagents, and controls for the duration of the study. Each operator performed the complete analysis of the OVA1™ Test for the day on the Siemens BN™ II System and on the Roche Elecsys® 2010 and imported the five biomarkers into Vermillion's OvaCalc Software for generation of the OVA1™ Test score. For each of the five specimens, the mean, SD, %CV, median, and range of OVA1™ Test scores were identified for an assessment of components of imprecision in reproducibility study. For OVA1™ Test scores, the %CV for within-run (repeatability) was ≤ 7.3, the %CV for between-run ≤2.4%, %CV between-day was ≤3.9%, the %CV between-operator ≤5.3% and the %CV between-site ≤4.4% . The total imprecision (reproducibility) was ≤8.9%. The results for the OVA1™ Test are shown below:

Parameters		Specimen				
		1	2	3	4	5
OVA1 result						
Mean		2.67	3.21	3.75	5.00	9.71
Repeatability (within run)	SD	0.069	0.094	0.157	0.364	0.157
	%CV	2.6	2.9	4.2	7.3	1.6
Between run	SD	0.034	0.087	0.091	0.000	0.129
	%CV	1.3	2.7	2.4	0.0	1.3
Between day	SD	0.000	0.000	0.146	0.032	0.045
	%CV	0.0	0.0	3.9	0.6	0.5
Between operator	SD	0.042	0.039	0.105	0.265	0.000

Parameters		Specimen				
		1	2	3	4	5
	%CV	1.6	1.2	2.8	5.3	0.0
Between sites	SD	0.057	0.141	0.000	0.103	0.212
	%CV	2.1	4.4	0.0	2.1	2.2
Reproducibility (total)	SD	0.098	0.176	0.250	0.447	0.271
	%CV	3.7	5.5	6.7	8.9	2.8
Individual Protein Biomarkers						
Apolipoprotein A1, mg/dL						
Mean		148.6	156.5	174.5	192.8	155.4
Repeatability (within run)	SD	4.489	4.702	3.438	5.840	4.091
	%CV	3.0	3.0	2.0	3.0	2.6
Between run	SD	2.058	0.000	4.221	0.000	3.456
	%CV	1.4	0.0	2.4	0.0	2.2
Between day	SD	3.105	3.075	3.227	4.969	1.622
	%CV	2.1	2.0	1.8	2.6	1.0
Between operator	SD	3.446	3.744	4.264	3.768	3.569
	%CV	2.3	2.4	2.4	2.0	2.3
Between sites	SD	6.535	6.338	6.733	5.570	6.408
	%CV	4.4	4.1	3.9	2.9	4.1
Reproducibility (total)	SD	8.513	8.377	9.240	9.525	8.340
	%CV	5.7	5.4	5.3	4.9	5.4
Beta-2 microglobulin, mg/L						
Mean		1.66	1.64	1.79	1.94	2.11
Repeatability (within run)	SD	0.046	0.039	0.045	0.040	0.053
	%CV	2.7	2.4	2.5	2.1	2.5
Between run	SD	0.055	0.028	0.036	0.025	0.011
	%CV	3.3	1.7	2.0	1.3	0.5
Between day	SD	0.000	0.015	0.038	0.025	0.034
	%CV	0.0	0.9	2.1	1.3	1.6
Between operator	SD	0.030	0.017	0.000	0.014	0.038
	%CV	1.8	1.1	0.0	0.7	1.8
Between sites	SD	0.029	0.024	0.027	0.026	0.018
	%CV	1.7	1.4	1.5	1.3	0.9
Reproducibility (total)	SD	0.080	0.056	0.072	0.059	0.074
	%CV	4.8	3.5	4.0	3.0	3.5

Parameters		Specimen				
		1	2	3	4	5
CA125 II, U/mL						
Mean		9.02	14.04	17.02	20.92	352.1
Repeatability (within run)	SD	0.354	0.210	0.839	0.525	5.131
	%CV	3.9	1.5	4.9	2.5	1.5
Between run	SD	0.176	0.590	0.679	1.054	20.53
	%CV	2.0	4.2	4.0	5.0	5.8
Between day	SD	0.140	0.176	0.386	0.000	5.054
	%CV	1.6	1.3	2.3	0.0	1.4
Between operator	SD	0.453	0.294	0.000	0.000	3.306
	%CV	5.0	2.1	0.0	0.0	0.9
Between sites	SD	0.476	0.380	0.138	0.236	5.182
	%CV	5.3	2.7	0.8	1.1	1.5
Reproducibility (total)	SD	0.708	0.766	1.146	1.187	22.22
	%CV	7.9	5.5	6.7	5.7	6.3
Transferrin, mg/dL						
Mean		270.9	263.3	290.2	308.4	280.4
Repeatability (within run)	SD	12.02	7.980	10.73	8.627	11.02
	%CV	4.4	3.0	3.7	2.8	3.9
Between run	SD	7.514	10.77	10.73	10.80	6.947
	%CV	2.8	4.1	3.7	3.5	2.5
Between day	SD	9.509	1.725	2.058	1.335	0.000
	%CV	3.5	0.7	0.7	0.4	0.0
Between operator	SD	0.000	0.992	4.799	4.587	1.581
	%CV	0.0	0.4	1.7	1.5	0.6
Between sites	SD	16.78	19.99	20.46	20.06	18.23
	%CV	6.2	7.6	7.1	6.5	6.5
Reproducibility (total)	SD	21.84	21.26	23.13	21.93	19.89
	%CV	8.1	8.1	8.0	7.1	7.1
Prealbumin (transthyretin), mg/dL						
Mean		21.48	25.04	29.33	34.78	24.78
Repeatability (within run)	SD	0.619	0.936	0.951	1.677	0.694
	%CV	2.9	3.7	3.2	4.8	2.8
Between run	SD	0.534	0.471	0.938	0.587	0.417
	%CV	2.5	1.9	3.2	1.7	1.7
Between day	SD	0.302	0.000	0.161	0.000	0.556

Parameters		Specimen				
		1	2	3	4	5
	%CV	1.4	0.0	0.5	0.0	2.2
Between operator	SD	0.574	0.432	0.510	0.979	0.848
	%CV	2.7	1.7	1.7	2.8	3.4
Between sites	SD	0.538	0.650	0.124	0.000	0.164
	%CV	2.5	2.6	0.4	0.0	0.7
Reproducibility (total)	SD	1.107	1.240	1.423	1.990	1.255
	%CV	5.2	5.0	4.9	5.7	5.1

b. *Linearity/assay reportable range:*
For each analyte, measurement linearity (as claimed in the package inserts for the individual analytes) was demonstrated for measurement intervals corresponding to those used in the OVA1™ Test.

c. *Traceability, Stability (controls, calibrators, or methods):*
Each assay uses its own calibrator and controls. The calibrator and control for β_2-microglobulin are traceable to WHO 1st International Preparation. For transferrin and prealbumin, the calibrators and controls are traceable to protein reference preparation CRM 470.

Stability – Closed Vial: For each assay, users are instructed to refer to the individual stability information in the package insert.

Stability - Open Vial: Studies were performed to investigate the stability of the reagents used in the OVA1™ Test and impact on the OVA1™ Test score when they are opened for use and stored at 2-8°C. Three (3) serum specimens spanning the OVA1™ Test score range (one low, one high and one at the cut-off) were tested in duplicate after opening reagents and storing at various time points. The data demonstrate open vial reagent stability is acceptable when stored after opening as follows: Four (4) weeks at 2-8°C for Apo A-1, Prealbumin, Transferrin, on the Siemens BNII, and six (6) weeks for CA 125 II on the Roche Elecsys® 2010. Stability of the β2M reagents once reconstituted is up to 1 week at 2-8°C. Calibrators and controls are stable up to 4 weeks at 2-8°C.

Specimen Stability: Serum samples from 10 healthy pre- and post-menopausal women were used to evaluate stability (consistency) of the OVA1™ Test scores. The mean, SD, median and range were used to describe the OVA1™ Test score and each of the 5 analyte values for each patient sample stored under each condition, at each time point in duplicate when compared to time point 0. Storage conditions consisted of room temperature (15-25°C) up to 48 hours, refrigerated (2-8°C) up to 9 days, and frozen (-15 to -35°C and -60 to -85°C) up to 13 weeks. The summary table below shows the mean change

from the initial result, the standard error (SE) and the 95% CI for the change, for the latest time interval. The results support the following specimen stability claims: fresh serum stored at +2 to +8°C can be used up to 8 days. Serum frozen within 24 hr at –20°C is stable up to 9 weeks. Serum frozen within 24 hours and stored at –65 to –85° is stable up to 12 weeks.

N=22	**15 to 25°C at 48 hours**	**2 to 8°C at 9 days**	**-15 to -35°C at 13 weeks**	**-60 to -85°C at 13 weeks**
OVA1™ Test				
Mean Change	0.03	0.05	0.01	-0.10
SE	0.038	0.039	0.056	0.037
95% CI	-0.04 to 0.10	-0.03 to 0.13	-0.10 to 0.12	-0.17 to -0.03
Apo A-1 (mg/dL)				
Mean Change	-0.05	1.05	1.18	3.82
SE	1.124	1.158	1.975	1.266
95% CI	-2.25 to 2.15	-1.22 to 3.32	-2.69 to 5.05	1.34 to 6.30
β2-microglobulin (mg/L)				
Mean Change	-04	-0.03	-0.01*	0.02*
SE	0.011	0.014	0.016	0.0.21
95% CI	-0.06 to 0.02	-0.05 to 0.00	0.04 to 0.03	-0.03 to 0.06
CA-125 II (U/mL)				
Mean Change	0.44	1.30	3.29	3.45
SE	0.097	0.173	0.094	0.08
95% CI	0.25 to 0.63	0.96 to 1.64	3.11 to 3.47	3.29 to 3.61
Transferrin (mg/dL)				
Mean Change	-9.09	-17.59	-2.5	-17.41
SE	2.053	2.425	2.827	2.245
95% CI	-13.11 to -5.07	-22.34 to -12.84	-8.04 to 3.04	-21.81 to -13.01
Prealbumin (mg/dL)				
Mean Change	0.39	0.08	-4.62	-2.94
SE	0.213	0.183	0.224	0.192
95% CI	-0.03 to 0.81	-0.28 to 0.44	-5.06 to -4.18	-3.32 to -2.56

*Data obtained at 4 weeks.

d. *Limit of Detection*
The limits of detection and limits of quantitation reported in each assay's package insert were confirmed and they are incorporated into the algorithm such that results outside of the measuring interval are not imported and do not yield an OVA1™ Test score.

e. *Analytical specificity:*
Interference: Three pooled serum samples with low (control score ~3.0), medium (control score ~4.5) and high (control score ~10.00) OVA1™ Test scores were evaluated for interference by hemoglobin, bilirubin (conjugated and unconjugated), triglycerides and rheumatoid factor. The effect of each interfering substance on the OVA1™ Test score was assessed using a mean of 4 repeated measurements on each sample and compared to control measurements. No significant interference at the concentrations evaluated

was observed on the OVA1™ Test score for any of the interferents evaluated except for rheumatoid factor. Specimens with rheumatoid factor greater than 250 RU/mL are not appropriate for the OVA1™ Test. Acceptance criteria for interference were < 10% difference between the sample with interferent and control.

Interferent	Substance Conc.	OVA1 (low)	OVA1 (med)	OVA1 (high)
		% difference from control		
Hemoglobin (g/L)	9.0	0.00	-1.06	0.00
Bilirubin (Conjugated) (g/L)	0.9	0.00	0.00	0.00
Bilirubin (Unconjugated) (g/L)	0.9	0.00	-0.54	0.00
Triglycerides (g/L)	5.0	-0.80	0.54	0.00
Rheumatoid Factor (IU/mL)	250	9.76	13.7	-0.75
	500	32.2	29.6	2.76
	1011	94.2	60.6	-15.3
	2500	44.5	35.7	-3.50

f. Assay cut-off:
See clinical cut-off

2. Comparison studies:
   a. Method comparison with predicate device:
   Not applicable
   b. Matrix comparison:
   Serum is the only claimed matrix for each of the 5 analytes evaluated.

3. Clinical studies:
   a. Clinical Sensitivity and Specificity:
   The OVA1™ Test score is based on 5 biomarkers (Prealbumin, Apo A-1, β_2M, Transferrin, and CA 125) measured individually as 5 immunoassays and incorporated into a single numerical score using an algorithm. The algorithm was derived using two independent training data sets from preoperative serum samples. The output of the algorithm is a numeric index between 0.0 and 10.0. Two cutoffs, 5.0 and 4.4 for pre- and post-menopausal patients respectively, were identified based on the training data. The cutoff score classifies a patient based on her OVA1™ Test score as low probability or high probability for presence of ovarian malignancy.

   Training set 1 consisted of 284 pre-operative serum samples from women with adnexal mass, obtained from the University of Kentucky: 175 benign diseases, 29 ovarian tumors of low malignant potential (LMP), 64 epithelial ovarian cancers, 3 other primary ovarian malignancies and 13 other

malignancies. Complete laboratory data was available for 274 samples of which 109 were malignant and 175 were benign controls. Training set 2 consisted of a randomly selected subset of 146 pre-operative serum samples collected under a collection/enrollment protocol from the clinical trial serum specimen repository. Twenty-one (21) of these samples were not evaluable. The remaining set of 125 consisted of 89 benign diseases, 10 LMPs, 19 epithelial ovarian cancers, 1 primary and 3 non-primary ovarian cancers and 3 other malignancies.

Clinical Validation Study:

The clinical validation study was a prospective, multicenter, double-blind clinical study. Study samples were collected from 27 demographically mixed subject enrollment sites that are representative of institutions where patients with ovarian masses typically undergo a complete clinical evaluation prior to surgical intervention. These sites included large and small medical centers (universities/community hospitals), small gynecology/obstetrics groups, gynecology/oncology practices, and subjects from HMO groups. Subjects were women over 18 with a documented pelvic mass following physical examination and clinical examination. Enrollment in the study was limited to those patients with planned surgical intervention. Patients who had a diagnosis of malignancy within the last 5 years with the exception of melanoma were excluded from the study. Pre-surgical assessments identifying the mass as benign or malignant were made based on a variety of clinical assessments. One imaging test was required and had to be performed within 12 weeks of surgery. Blinded sample testing was conducted at 3 laboratories using bar-coded serum aliquots. The OVA1™ Test results, in conjunction with other clinicopathologic variables (e.g., patient's symptoms, physical findings, imaging, CA-125 value), were compared to histopathology results for detecting the presence of ovarian malignancy.

A total of 743 patients were enrolled in the study. A total of 146 subjects were set aside as a training set (as described above). Seventy-four (74) subjects/specimens were eliminated due to missing information or lack of sample resulting in a final total of 516 evaluable subjects/samples. Menopausal status was self-reported. In cases where menopausal status was not identified, a cut off of 50 years of age was applied. A pre-surgical clinical assessment based on radiological findings and other clinical data was obtained by the physician for each patient.

OVA1™ Test score cut points for negative versus positive test result were as follows:

Pre-menopausal:

low probability for malignancy	OVA1™ Test score < 5.0
high probability for malignancy	OVA1™ Test score ≥ 5.0

Post-menopausal:

low probability for malignancy	OVA1™ Test score < 4.4
high probability for malignancy	OVA1™ Test score ≥ 4.4

Summary statistics for enrolled subjects (age, menopausal status, and pathology) for all evaluable patients are in the following Table. For 269 patients, the pre-surgical evaluations were made by physicians who are not gynecologic oncologists (non-GO, i.e., gynecologists and primary care physicians). For 247 patients, the pre-surgical evaluations were made by gynecologic oncologists (GO). The demographic and outcome data are presented for all patients and for the two pre-surgical evaluation subsets.

Demographic Characteristics and Pathology Results for Evaluable Subjects with a Presurgical Clinical Assessment

	All Evaluable Subjects with Presurgical Assessment (N= 516)	Subjects with Evaluation by Non-GO Physicians (N= 269)	Subjects with Evaluation by GO Physicians (N= 247)
Age, years			
N	516	269	247
Mean (SD)	52.0 (13.9)	49.7 (13.6)	54.6 (13.8)
Range (min, max)	18 to 92	19 to 90	18 to 92
Menopausal Status, n (%)			
Pre	235 (45.5%)	144 (53.5%)	91 (36.8%)
Post	281 (54.5%)	125 (46.5%)	156 (63.2%)
Pathology Diagnosis, n (%)			
Benign ovarian conditions	355 (68.8%)	197 (73.2%)	158 (64.0%)
Epithelial ovarian cancer	96 (18.6%)	45 (16.7%)	51 (20.6%)
Other primary ovarian malignancies (not EOC)	9 (1.7%)	5 (1.9%)	4 (1.6%)
Low malignant potential (Borderline)	28 (5.4%)	12 (4.5%)	16 (6.5%)
Non-primary ovarian malignancies with involvement of the ovaries	18 (3.5%)	5 (1.9%)	13 (5.3%)
Non-primary ovarian malignancies with no involvement of ovaries	10 (1.9%)	5 (1.9%)	5 (2.0%)

All major racial groups were represented (21.7% (128/590) of subjects from ethnic groups).

For the 105 surgically confirmed cases of primary ovarian malignancy, 99 had tumor grade information (11 grade 1, 25 grade II, and 63 grade III), and 103 had stage information (31 stage I, 18 stage II, 51 stage III, and 3 stage IV). Summary statistics for OVA1™ Test scores in these patients are given by stage in the table below.

OVA1™ Test scores for the 105 EOC and non-EOC primary ovarian malignancies by stage:

	Stage I	Stage II	Stage III	Stage IV	Not Given
No. of Subjects	31	18	51	3	2
OVA1 Score Mean (SD)	6.48 (1.786)	8.04 (1.596)	8.26 (1.357)	8.70 (1.054)	6.05 (1.626)
Median	6.30	8.60	8.80	8.60	6.05
Range (min, max)	3.6 to 10.0	5.0 to 10.0	5.0 to 10.0	7.7 to 9.8	4.9 and 7.2

The distribution of histological classifications for the 105 patients with primary malignant ovarian tumors included fifty-five (55) serous, eight (8) mucinous, ten (10) endometroid, eight(8) clear cell, and twenty-four (24) other.

Performance Characteristics of the OVA1™ Test as Used by Physicians Who Are Not Gynecologic Oncologists (non-GO):

From a total of 516 evaluable subjects, 269 patients (age range 19-90) were evaluated by physicians who are not gynecologic oncologists (non-GO, i.e., gynecologists and primary care physicians). Of the 269 patients, 144 subjects were identified as pre-menopausal and 125 as post-menopausal.

For each patient, the OVA1™ Test result was compared to the pathology report from tissue. Malignant masses were those that included epithelial ovarian cancer (EOC), ovarian tumor of low malignant potential (LMP), other ovarian primary malignancy, malignancy involving but not arising in the ovary, and malignancy neither involving nor arising in the ovary, The table below shows performance characteristics of the OVA1™ Test alone for all subjects evaluated by non-GO, and separately for pre-menopausal and post-menopausal subjects. NPV denotes negative predictive value, and PPV denotes positive predictive value.

Performance of OVA1™ Test Alone Compared to Histopathology in Patients Evaluated by Non-GO			
	All	Pre-menopausal	Post-menopausal
N	269	144	125
Sensitivity 95% CI	87.5% (63/72) 77.9% - 93.3%	80.8% (21/26) 62.1% - 91.5%	91.3% (42/46) 79.7% - 96.6%
Specificity 95% CI	50.8% (100/197) 43.8% - 57.7%	56.8% (67/118) 47.8% - 65.4%	41.8% (33/79) 31.5% - 52.8%
NPV	91.7% (100/109)	93.1% (67/72)	89.2% (33/37)
PPV	39.4% (63/160)	29.2% (21/72)	47.7% (42/88)
Prevalence	26.8% (72/269)	18.1% (26/144)	36.8% (46/125)

In order to conclude that the test is statistically informative, it is necessary to demonstrate that the TPR (True Positive Rate, same as Sensitivity) differs from the FPR (False Positive Rate, same as 1 – Specificity). For a non-informative test (a random test, no better than the toss of a coin), the percent of positive test results does not depend on whether a subject has a target condition or not (TPR = FPR).

The OVA1™ Test was statistically informative for the combined data and for pre-menopausal and post-menopausal subjects separately.

- The True Positive Rate (TPR) exceeded the False Positive Rate (FPR) for all combined data: the estimate of TPR was 87.5% (63/72) and the estimate of FPR was 49.2% (97/197); the difference of TPR and FPR was statistically significant (38.3% with 95% CI: 26.5% to 47.8%).
- The TPR exceeded the FPR for the pre-menopausal subjects: the estimate of TPR was 80.8% (21/26) and the estimate of FPR was 43.2% (51/118); the difference of TPR and FPR was statistically significant (37.6% with 95% CI: 16.7% to 52.2%).
- The TPR exceeded FPR for the post-menopausal subjects: the estimate of TPR was 91.3% (42/46) and the estimate of FPR was 58.2% (46/79); the difference of TPR and FPR was statistically significant (33.1% with 95% CI: 17.3% to 46.1%).

The information provided by the OVA1™ Test should be used by the physician only as an adjunctive test to complement, not replace, other diagnostic and clinical procedures. To examine whether the OVA1™ Test provides additional information when used in combination with the physician's pre-surgical assessment, the ability to contribute to the physician's pre-surgical assessment was analyzed.

The analysis examined whether patient referral to a gynecological oncologist is supported when positive OVA1™ Test results occur in the setting of negative clinical evaluations by non-GO physicians. The mass was declared potentially malignant if the pre-surgical clinical assessment, the OVA1™ Test score, or both were positive.

In the study, there were 269 subjects:

- 24.1% (65/269) were subjects with "Positive" Pre-surgical assessment and positive OVA1™ Test results,
- 7.8% (21/269) were subjects with "Positive" Pre-surgical assessment and negative OVA1™ Test results,
- 35.3% (95/269) were subjects with "Negative" Pre-surgical assessment and positive OVA1™ Test results, and
- 32.7% (88/269) were subjects with "Negative" Pre-surgical assessment and negative OVA1™ Test results.

		Non-GO Pre-surgical Assessment		
		Positive	**Negative**	Total
OVA1	**Positive**	65	95	160
	Negative	21	88	109
	Total	86	183	269

Among 269 subjects, there were 72 subjects with malignancy by pathology and 197 subjects with no malignancy by pathology.

Malignancy by Pathology				
		Non-GO Pre-surgical Assessment		
		Positive	**Negative**	Total
OVA1	**Positive**	49	14	63
	Negative	3	6	9
	Total	52	20	72

No Malignancy by Pathology				
		Non-GO Pre-surgical Assessment		
		Positive	**Negative**	Total
OVA1	**Positive**	16	81	97
	Negative	18	82	100
	Total	34	163	197

The following table presents the observed frequencies of malignancy tabulated according to pre-surgical evaluation and OVA1™ Test results from the 269 patients evaluated by non-GO physicians:

	Frequency of Malignancy	95% CI
Prevalence of malignancy among patients with adnexal mass assessed by non-GO physicians: 26.8% (72/269)		
Pre-surgical assessment alone "Positive"	60.5% (52/86)	49.9% to 70.1%
Pre-surgical assessment alone "Negative"	10.9% (20/183)	7.2% to 16.3%
OVA1™ Test Score alone "Positive"	39.4% (63/160)	32.1% to 47.1%
OVA1™ Test Score alone "Negative"	8.3% (9/109)	4.4% to 15.0%
Pre-surgical assessment "Positive" and OVA1™ Test Score "Positive"	75.4% (49/65)	63.7% to 84.2%
Pre-surgical assessment "Positive" and OVA1™ Test Score "Negative"	14.3% (3/21)	5.0% to 34.6%
Pre-surgical assessment "Negative" and OVA1™ Test Score "Positive"	14.7% (14/95)	9.0% to 23.2%
Pre-surgical assessment "Negative" and OVA1™ Test Score "Negative"	6.8% (6/88)	3.2% to 14.1%

The same information about the frequencies of malignancy can be presented also by the likelihood ratios: Likelihood ratio (Result) = Pr(Result|Malignancy) / Pr(Result|No Malignancy). Likelihood ratio is a way of quantifying how much a given test result changes the pre-test probability of malignancy in a patient.

Results for Patient	Likelihood Ratio
Pre-surgical assessment alone "Positive"	4.18
Pre-surgical assessment alone "Negative"	0.34
OVA1™ Test Score alone "Positive"	1.78
OVA1™ Test Score alone "Negative"	0.25
Pre-surgical assessment "Positive" and OVA1™ Test Score "Positive"	8.37
Pre-surgical assessment "Positive" and OVA1™ Test Score "Negative"	0.46
Pre-surgical assessment "Negative" and OVA1™ Test Score "Positive"	0.47
Pre-surgical assessment "Negative" and OVA1™ Test Score "Negative"	0.20

The Table below shows performance characteristics for the test applied to all subjects evaluated by non-GO physicians. For Single Assessment, only the pre-surgical assessment was used, without reference to an OVA1™ Test result. For Dual Assessment, the adnexal mass was declared potentially malignant if the pre-surgical clinical assessment, the OVA1™ Test score, or both were positive.

Performance	Single Assessment (Pre-surgical Assessment)	Dual Assessment (Pre-surgical Assessment and OVA1™ Test)
Sensitivity	72.2% (52/72)	91.7% (66/72)
Specificity	82.7% (163/197)	41.6% (82/197)
PPV	60.5% (52/86)	36.5% (66/181)
NPV	89.1% (163/183)	93.2% (82/88)
Prevalence	26.8% (72/269)	

With dual assessments, sensitivity for malignancy increased from 72% to 92%. That is, approximately two-thirds of the malignancies missed by pre-surgical assessment alone were called positive when a dual assessment was used. Specificity for malignancy decreased from 83% to 42% with dual assessment. The ratio of false positive results to true positive results for the study population increased from 34:52 (0.65:1) with single assessment to 115:66 (1.74:1) with dual assessment (PPV with dual assessment decreased from 60% to 37%). However, NPV with dual assessment increased from 89% to 93%, supporting improved performance with dual assessment. The confidence interval for the observed 4.1% increase was -0.5% to 8.7% (calculated by bootstrap). The statistical significance of the observed increase in NPV was borderline.

For the already surgery-bound intended use population, the additional true positive cases detected by dual assessment present a sufficient benefit (in terms of opportunity for optimal treatment) compared to the additional false positive cases (for which an unneeded referral poses no medical risk to the patients).

Pre-menopausal subjects

Among 144 pre-menopausal subjects, with pre-surgical assessment by a non-GO, there were 26 subjects with malignancy by pathology and 118 subjects with no malignancy by pathology.

Malignancy by Pathology				
		Non-GO Pre-surgical Assessment		
		Positive	Negative	Total
OVA1	Positive	16	5	21
	Negative	1	4	5
	Total	17	9	26

No Malignancy by Pathology				
		Non-GO Pre-surgical Assessment		
		Positive	**Negative**	Total
OVA1	**Positive**	7	44	51
	Negative	13	54	67
	Total	20	98	118

Performance	**Single Assessment (Pre-surgical Assessment)**	**Dual Assessment (Pre-surgical Assessment and OVA1™ Test)**
Sensitivity	65.4% (17/26)	84.6% (22/26)
Specificity	83.1% (98/118)	45.8% (54/118)
PPV	45.9% (17/37)	25.6% (22/86)
NPV	91.6% (98/107)	93.1% (54/58)
Prevalence	18.1% (26/144)	

PPV of the dual assessment decreased from 46% to 26% and NPV of the dual assessment increased from 92% to 93%. The confidence interval for the observed 1.5% increase was -3.3% to 6.4% (calculated by bootstrap).

Post-menopausal subjects

Among 125 post-menopausal subjects, there were 46 subjects with malignancy by pathology and 79 subjects with no malignancy by pathology.

Malignancy by Pathology				
		Non-GO Pre-surgical Assessment		
		Positive	**Negative**	Total
OVA1	**Positive**	33	9	42
	Negative	2	2	4
	Total	35	11	46

No Malignancy by Pathology				
		Non-GO Pre-surgical Assessment		
		Positive	**Negative**	Total
OVA1	**Positive**	9	37	46
	Negative	5	28	33
	Total	14	65	79

Performance	Single Assessment (Pre-surgical Assessment)	Dual Assessment (Pre-surgical Assessment and OVA1™ Test)
Sensitivity	76.1% (35/46)	95.7% (44/46)
Specificity	82.3% (65/79)	35.4% (28/79)
PPV	71.4% (35/49)	46.3% (44/95)
NPV	85.5% (65/76)	93.3% (28/30)
Prevalence	36.8% (46/125)	

PPV of the dual assessment decreased from 72% to 46% and NPV of the dual assessment increased from 86% to 93%. The confidence interval for the observed 7.8% increase was -1.6% to 17.2% (calculated by bootstrap).

Summary statistics for OVA1™ Test scores, for subjects who were both evaluated by a non-GO physician and had a primary ovarian malignancy (EOC and non-EOC), are given by cancer stage in the table below. There were no Stage IV cancers among these patients.

Table # OVA1™ Test Scores by Cancer Stage for primary ovarian malignancies in All Evaluable Subjects with a Pre-surgical Clinical Assessment from Non-GO

	Stage I	Stage II	Stage III
No. of Subjects	14	11	25
OVA1 Mean (SD)	6.89 (2.313)	8.21 (1.600)	8.36 (1.289)
Median	6.55	8.60	8.70
Range (min, max)	3.6 to 10.0	5.1 to 10.0	5.5 to 10.0
OVA1 Positive	11	11	25
OVA1 Negative	3	0	0
OVA1 Sensitivity	78.6 %	100%	100%

Performance Characteristics of the OVA1™ Test as Used by Gynecologic-Oncologists (GO):

The characteristics of patients evaluated by GO differ from those of patients evaluated by non-GO physicians. Due to selective referral, the prevalence of malignancy is typically higher for adnexal masses in patients who are evaluated by GO, and malignancy found at surgery for these patients may be higher stage disease which can impact test performance characteristics. In addition, the spectrum of disease (i.e., the kind and frequency of benign adnexal masses) may vary between GO and non-GO settings and impact the

performance characteristics of the test. As a result, performance characteristics within already-referred patients may corroborate, but are insufficient to establish, performance characteristics in a not-yet-referred patient population.

There were 247 patients evaluated by gynecologic oncologists in the OVA1™ Test clinical study, with 91 premenopausal and 156 postmenopausal subjects. The Table below presents results for all subjects evaluated by GO and separately by menopausal status for pre-menopausal and post-menopausal subjects.

Performance of OVA1™ Test compared to Histology in patients Evaluated by GO			
	All	Pre-menopausal	Post-menopausal
N	247	91	156
Sensitivity (95% CI)	96.6% (86/89) 90.6% - 98.9%	94.7% (18/19) 75.4% – 99.1%	97.1% (68/70) 90.2% -99.2%
Specificity (95% CI)	32.9% (52/158) 26.1% – 40.6%	43.1% (31/72) 32.2% - 54.6%	24.4% (21/86) 16.6% - 34.5%
NPV	94.5% (52/55)	96.9% (31/32)	91.3% (21/23)
PPV	44.8% (86/192)	30.5% (18/59)	51.1% (68/133)
Prevalence	36.0% (89/247)	20.9% (19/91)	44.9% (70/156)

For the patients evaluated by gynecologic oncologists, the observed positive likelihood ratio (PLR) was 1.44 and the observed negative likelihood ratio (NLR) was 0.10; for the patients evaluated by non-GO physicians, PLR was 1.78 and NLR was 0.25. Sensitivity of the OVA1™ Test was notably higher, and specificity was notably lower, for GO-evaluated patients compared to non-GO-evaluated patients. Nevertheless, the NPV and PPV figures were slightly higher in the GO-evaluated patients (predictive values depend on the corresponding likelihood ratios and prevalence).

Analyses combining pre-surgical assessment with the OVA1™ Test result were completed for GO-evaluated patients, echoing the analyses performed for patients evaluated by non-GO physicians. The results are corroborative, but are not dispositive, concerning safety and effectiveness of the test for the intended use population.

		GO Pre-surgical Assessment		
		Positive	**Negative**	Total
OVA1	**Positive**	96	96	192
	Negative	13	42	55
	Total	109	138	247

Among 247 subjects, there were 89 subjects with malignancy by pathology and 158 subjects with no malignancy by pathology.

Malignancy by Pathology				
		GO Pre-surgical Assessment		
		Positive	**Negative**	Total
OVA1	**Positive**	67	19	86
	Negative	2	1	3
	Total	69	20	89

No Malignancy by Pathology				
		GO Pre-surgical Assessment		
		Positive	**Negative**	Total
OVA1	**Positive**	29	77	106
	Negative	11	41	52
	Total	40	118	158

The following table presents the observed frequencies of malignancy tabulated according to pre-surgical evaluation and OVA1™ Test results from the 247 patients evaluated by gynecologic oncologists:

	Frequency of Malignancy	**95% CI**
Prevalence of malignancy among patients with adnexal mass assessed by gynecologic oncologists: 36.0% (89/247)		
Pre-surgical assessment alone "Positive"	63.3% (69/109)	53.9% to 71.8%
Pre-surgical assessment alone "Negative"	14.5% (20/138)	9.6% to 21.3%
OVA1™ Test Score alone "Positive"	44.8% (86/192)	37.9% to 51.9%
OVA1™ Test Score alone "Negative"	5.5% (3/55)	1.9% to 14.9%
Pre-surgical assessment "Positive" and OVA1™ Test Score "Positive"	69.8% (67/96)	60.0% to 78.1%
Pre-surgical assessment "Positive" and OVA1™ Test Score "Negative"	15.4% (2/13)	4.3% to 42.2%
Pre-surgical assessment "Negative" and OVA1™ Test Score "Positive"	19.8% (19/96)	13.1% to 28.9%
Pre-surgical assessment "Negative" and OVA1™ Test Score "Negative"	2.4% (1/42)	0.4% to 12.3%

The same information about the frequencies of malignancy is presented also by the

observed likelihood ratios:

Results for Patient	Likelihood Ratio
Pre-surgical assessment alone "Positive"	3.06
Pre-surgical assessment alone "Negative"	0.30
OVA1™ Test Score alone "Positive"	1.44
OVA1™ Test Score alone "Negative"	0.10
Pre-surgical assessment "Positive" and OVA1™ Test Score "Positive"	4.10
Pre-surgical assessment "Positive" and OVA1™ Test Score "Negative"	0.32
Pre-surgical assessment "Negative" and OVA1™ Test Score "Positive"	0.44
Pre-surgical assessment "Negative" and OVA1™ Test Score "Negative"	0.04

The Table below shows results for all subjects evaluated by gynecological oncologists, with conclusions for malignancy either based on a positive pre-surgical assessment alone (single assessment), or based on a positive result from the pre-surgical assessment or from the OVA1™ Test result or from both (dual assessment).

Performance	Single Assessment (Pre-surgical Assessment)	Dual Assessment (Pre-surgical Assessment and OVA1™ Test)
Sensitivity	77.5% (69/89)	98.9% (88/89)
Specificity	74.7% (118/158)	25.9% (41/158)
PPV	63.3% (69/109)	42.9% (88/205)
NPV	85.5% (118/138)	97.6% (41/42)
Prevalence	36.0% (89/247)	

With dual assessments, sensitivity for malignancy increased from 77% to 99% and specificity for malignant calls decreased from 75% to 26% with dual assessment. Also with dual assessment, the PPV decreased from 63% to 43%, and the NPV increased from 86% to 98%. The confidence interval for the observed 12.1% increase in NPV was 5.7% to 18.6% (calculated by bootstrap). The observed increase in NPV was statistically significant.

Summary statistics for OVA1™ Test scores, for subjects who were both evaluated by a gynecologic oncologist and had a primary ovarian malignancy (EOC and non-EOC) are given by cancer stage in the table below:

Table # OVA1™ Test Scores by Cancer Stage for Evaluable Subjects with a Pre-surgical Clinical Assessment from Gynecologic Oncologists

	Stage I	Stage II	Stage III	Stage IV	Not Given
No. of Subjects	17	7	26	3	2
OVA1 Mean (SD)	6.14 (1.167)	7.79 (1.681)	8.17 (1.439)	8.70 (1.054)	6.05 (1.626)
Median	6.30	8.60	8.85	8.60	6.05
Range (min,max)	4.4 to 7.9	5.0 to 9.8	5.0 to 10.0	7.7 to 9.8	4.9 and 7.2
OVA1 Positive	17	7	26	3	2
OVA1 Negative	0	0	0	0	0
Sensitivity (%)	100	100	100	100	100

b. Other clinical supportive data (when a is not applicable):
Not applicable.

4. Clinical cut-off**:**
The results are interpreted as follows:

Pre-menopausal:

low probability for malignancy	OVA1™ Test score < 5.0
high probability for malignancy	OVA1™ Test score ≥ 5.0

Post-menopausal:

low probability for malignancy	OVA1™ Test score < 4.4
high probability for malignancy	OVA1™ Test score ≥ 4.4

5. Expected values/Reference interval:
To determine the reference interval of OVA1™ Test in healthy women, 69 pre-menopausal patients and 78 post-menopausal patients were tested (total = 147 evaluable subjects). Ages ranged from 18 to 85 and represented whites (81.3%), Hispanic/Latino (8.7%) and African American (7.3%) subjects. Using a cut-off of 5.0 for OVA1™ Test scores, the results from the pre- and post-menopausal populations are presented below:

	All Evaluable Subjects (N= 147)	Pre-menopausal Subjects (N= 69)	Post-menopausal Subjects (N= 78)
N	147	69	78
OVA1™ Test Score			
Mean (SD)	4.18 (0.858)	4.34 (0.871)	4.04 (0.827)
Median	4.10	4.30	3.95
Range (min, max)	2.7, 6.7	2.9, 6.7	2.7, 6.1
Reference interval (5th percentile, 95th percentile)	(3.0, 5.8)	(3.0, 5.8)	(2.9, 5.9)
OVA1™ Test Score' n (%)			
Positive	46 (31.3%)	20 (29.0%)	26 (33.3%)
Negative	101 (68.7%)	49 (71.0%)	52 (66.7%)

Expected Values in Non-Ovarian Malignancy Condition: To evaluate the performance of the OVA1™ Test in subjects with other benign and malignant conditions, the OVA1™ Test was evaluated in subjects with (breast cancer, Stage 1 to Stage IV; endometrial cancer, cervical cancer, bladder cancer, lung cancer, colon cancer, leukemia and lymphoma) and in women with benign conditions (anemia of chronic disease, iron deficiency anemia, acute and chronic pelvic inflammatory disease, malnutrition, cardiac disease, hepatitis, kidney diseases and autoimmune disease). A total of 360 evaluable specimens were analyzed.

	Evaluable specimens
All Specimens	360
Bladder cancer	16
Breast cancer	45
Cervical cancer	12
Colon cancer	40
Endometrial cancer	44
Leukemia	10
Lung cancer	13
Lymphoma	13
Autoimmune disease	10
Cardiac disease	12
Diabetes	40
Endometriosis	40

	Evaluable specimens
Hepatitis	13
Kidney disease	12
Pregnant women	10
Anemia	11
Pelvic inflammatory disease	9
Malnutrition	10

The mean, standard deviation, 5th to 95th percentiles as observed in the data are shown for each condition group. Using a cut-off of 5.0 for OVA1™ Test scores, the number of positive and negative cases is presented below:

Summary of OVA1™ Scores for Specimens from Subjects with Cancer Conditions

	Bladder Cancer (N= 16)	Breast Cancer (N= 45)	Cervical Cancer (N= 12)	Colon Cancer (N= 40)	Endometrial Cancer (N= 44)	Leukemia (N= 10)	Lung Cancer (N= 13)	Lymphoma (N= 13)
OVA1™ Test Score, statistics								
N	16	45	12	40	44	10	13	13
Mean (SD)	4.57 (1.109)	4.34 (1.151)	6.40 (1.979)	4.86 (1.259)	5.00 (1.467)	6.04 (0.651)	4.17 (0.884)	5.26 (1.669)
Median	4.4	4.1	6.6	4.8	4.6	6.1	4.0	4.6
5th to 95th percentiles	2.9 to 6.5	2.9 to 6.0	3.4 to 9.8	3.0 to 7.0	3.5 to 8.3	4.6 to 7.0	3.0 to 5.5	3.0 to 8.6
OVA1™ Test Score, n								
Positive	6	11	8	18	15	9	3	6
Negative	10	34	4	22	29	1	10	7
% negative results	62.5	75.6	33.3	55.0	65.9	10.0	76.9	53.8

Summary of OVA1 Scores for Specimens from Subjects with Non-cancer Conditions

	Autoimmune Disease (N= 10)	Cardiac Disease (N= 12)	Diabetes (N= 40)	Endo-metriosis (N= 40)	Hepatitis (N= 13)
OVA1™ Test Score, statistics					
N	10	12	40	40	13
Mean (SD)	5.23 (1.083)	5.28 (1.345)	4.39 (1.069)	5.01 (1.189)	4.46 (0.832)
Median	5.3	5.6	4.0	4.7	4.2
5th to 95th percentiles	3.4 to 6.6	3.3 to 8.0	3.2 to 6.4	3.4 to 7.1	3.5 to 6.0

	Autoimmune Disease (N= 10)	Cardiac Disease (N= 12)	Diabetes (N= 40)	Endo-metriosis (N= 40)	Hepatitis (N= 13)
OVA1™ Test Score, n					
Positive	5	7	10	17	3
Negative	5	5	30	23	10
%negative results	50.0	41.7	75.0	57.5	76.9

	Kidney Disease (N= 12)	Pregnant Women (N= 10)	Anemia (N= 11)	Pelvic inflammatory disease (N= 9)	Malnutrition (N= 10)
OVA1™ Test Score, statistics					
N	12	10	11	9	10
Mean (SD)	6.13 (0.094)	4.86 (0.686)	3.73 (0.673)	4.52 (1.072)	4.30 (0.948)
Median	6.2	4.8	4.0	4.4	4.4
5^{th} to 95^{th} percentiles	5.9 to 6.2	4.0 to 6.2	2.7 to 4.7	3.2 to 6.3	2.8 to 5.7
OVA1™ Test Score, n					
Positive	12	3	0	2	2
Negative	0	7	11	7	8
%negative results	0.0	70.0	100	77.8	80.0

The number of cases is small within each of the examined diseases and conditions, but the results suggest that caution is warranted when interpreting OVA1™ Test results for patients with cervical cancer, leukemia, kidney disease and anemia.

N. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

O. Conclusion:

The petition for Evaluation of Automatic Class III Designation for this device is accepted. The device is classified as Class II under regulation 21 CFR 866.6050 with special controls. The special control guidance document, "Class II Special Controls Guidance Document: Ovarian Adnexal Mass Assessment Score Test System" accompanies this device.