DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
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July 7, 2015

THERANOS, INC.
BRAD ARINGTON
ASSOCIATE DIRECTOR, REGULATORY
1701 PAGE MILL ROAD
PALO ALTO, CA 94304

Re: K143236
Trade/Device Name: Theranos Herpes Simplex Virus-1 IgG Assay
Regulation Number: 21 CFR 866.3305
Regulation Name: Herpes simplex virus serological assays
Regulatory Class: II
Product Code: MXJ
Dated: June 29, 2015
Received: June 30, 2015

Dear Mr. Arington:

This letter corrects our substantially equivalent letter of July 2, 2015.

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 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 Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulations (21 CFR Parts 801 and 809), please contact the Division of Industry and Consumer Education at its toll-free number (800) 638 2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm. 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.

You may obtain other general information on your responsibilities under the Act from the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely yours,

Sally A. Hojvat -S

Sally A. Hojvat, M.Sc., Ph.D.
Director
Division of Microbiology Devices
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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: January 31, 2017
See PRA Statement below.

510(k) Number *(if known)*
K143236

Device Name
Theranos Herpes Simplex Virus-1 IgG Assay

Indications for Use *(Describe)*
The Theranos™ HSV-1 IgG Assay is a chemiluminescent immunoassay intended for the qualitative detection of IgG antibodies to herpes simplex virus type 1 (HSV-l) in human serum, in K2-EDTA anticoagulated human plasma from venous blood, and in human fingerstick K2-EDTA anticoagulated whole blood obtained with the Theranos Capillary Tubes and Nanotainer Tubes. The test is indicated for sexually active individuals and expectant mothers as an aid in the presumptive diagnosis of HSV-l infection. The predictive value of positive and negative results depends on the population's prevalence and the pretest likelihood of HSV-1.

The test is not FDA cleared for screening blood or plasma donors. The performance of this assay has not been established for use in a pediatric population, neonates and immunocompromised patients.

The Theranos HSV-1 IgG Assay is for use with the Theranos System which performs automated sample processing steps and result analysis.

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 K143236

I. GENERAL INFORMATION

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Date Prepared: June 29, 2015

II. DEVICE INFORMATION

Trade Name:	Theranos™ Herpes Simplex Virus-1 (HSV-1) IgG Assay
Common Name:	HSV-1 IgG assay
Regulation Number:	21 CFR§866.3305
Regulation Name:	Herpes simplex virus serological assays
Regulatory Class:	Class II
Product Code:	MXJ (Enzyme Linked Immunosorbent Assay, Herpes Simplex Virus, HSV-1)
Panel:	Microbiology (83)

III. PREDICATE DEVICE

HerpeSelect® 1 and 2 Immunoblot IgG (K000238; Focus Diagnostics, Inc.)

IV. DEVICE DESCRIPTION

The Theranos HSV-1 IgG Assay is for use with the Theranos System. The Theranos System performs automated sample processing steps and analysis to produce the test results.

The Theranos HSV-1 IgG Assay is a three-step sandwich immunoassay with an HSV-1 glycoprotein G (gG) recombinant antigen coated surface, an anti-human IgG detection reagent conjugated to alkaline phosphatase (AP) and chemiluminescent substrate. During the first incubation step, the HSV-1 IgG antibodies present in the positive control and sample bind to the gG recombinant antigen on the coated surface. Following the first incubation step, unbound materials are removed with a wash cycle. Then the detection reagent-AP conjugate is added and during the second incubation step, the detection reagent-AP conjugate reacts with the HSV-1 IgG antibodies already bound to the capture surface. Following the second incubation, unbound materials are removed with a wash cycle. The chemiluminescent substrate is added to the capture-analyte-detection complex during the third incubation step to initiate the chemiluminescence reaction. Light generated by this reaction is detected and analyzed by the Theranos System using a calibration function to determine the cut-off index (COI) values for the sample and controls. The results for the Positive and Negative controls must be within specified limits for a run to be considered valid.

V. INDICATIONS FOR USE

The Theranos™ HSV-1 IgG Assay is a chemiluminescent immunoassay intended for the qualitative detection of IgG antibodies to herpes simplex virus type 1 (HSV-l) in human serum, in K2-EDTA anticoagulated human plasma from venous blood, and in human fingerstick K2-EDTA anticoagulated whole blood obtained with the Theranos Capillary Tubes and Nanotainer Tubes. The test is indicated for sexually active individuals and expectant mothers as an aid in the presumptive diagnosis of HSV-l infection. The predictive value of positive and negative results depends on the population's prevalence and the pretest likelihood of HSV-1.

The test is not FDA cleared for screening blood or plasma donors. The performance of this assay has not been established for use in a pediatric population, neonates and immunocompromised patients.

The Theranos HSV-1 IgG Assay is for use with the Theranos System which performs automated sample processing steps and result analysis.

VI. COMPARISON OF TECHNOLOGICAL CHARACTERISTICS WITH THE PREDICATE DEVICE

Table 1: Similarities between the Theranos HSV-1 IgG Assay and the Predicate

Characteristic	Theranos™ HSV-1 IgG Assay **(K143236)**	Focus HerpeSelect® 1 and 2 Immunoblot IgG **(K000238)**
Intended use	Qualitative test to detect presence or absence of IgG antibodies to HSV-1 in human serum, in K2-EDTA anticoagulated human plasma from venous blood, and in human fingerstick K2-EDTA anticoagulated whole blood obtained with the Theranos Capillary Tubes and Nanotainer Tubes. Indicated for testing sexually active individuals and expectant mothers as an aid in presumptive diagnosis of HSV-1 infection. The predictive value of positive or negative results depends on the population's prevalence and the pretest likelihood of HSV-1 infection.	Qualitative test to detect presence or absence of IgG antibodies to HSV-1 and HSV-2 in human sera. Indicated for testing sexually active adults or expectant mothers as an aid in presumptive diagnosis of HSV-1 and HSV-2 infection. The predictive value of positive or negative results depends on the population's prevalence and the pretest likelihood of HSV-1 and HSV-2 infection.

Table 2: Differences between the Theranos HSV-1 IgG Assay and the Predicate

Characteristic	Theranos™ HSV-1 IgG Assay **(K143236)**	Focus HerpeSelect® 1 and 2 Immunoblot IgG **(K000238)**
Specimen Types	• Venous serum, • K2-EDTA anticoagulated human plasma from venous blood, • Human fingerstick K2-EDTA anticoagulated whole blood obtained with the Theranos Capillary Tubes and Nanotainer Tubes	• Venous Serum
Type of Assay	Chemiluminescent immunoassay	Nitrocellulose Immunoblot
Sample Handling	Automated sample handling/processing	Manual sample handling/processing
Capture Reagent	HSV-1 recombinant antigen (gG1)	HSV-1/HSV-2 antigen immobilized on nitrocellulose membrane

VII. PERFORMANCE

To characterize performance of the Theranos HSV-1 IgG immunoassay the following studies were conducted:

Precision – CLIA Laboratory Model, Venous Serum

A study for estimating the precision of the Theranos HSV-1 IgG Assay for venous serum samples in a CLIA Laboratory model was performed by testing a panel of 6 serum samples spanning the analytical range [negative (A), high negative (B), equivocal (C), low positive (D), moderate positive (E), and positive (F)]. The precision study was conducted at one site with thirty five (35) TSPU devices, three (3) lots of cartridges and sixteen (16) operators in total. The study duration was 13 days in total. Details of the study design for different samples are presented in Table 3 below.

Table 3: Design of Precision Study: Numbers of Replicates, Devices, Days and Operators

Panel Member	Valid Replicates				No. of Devices	No. of Days	No. of Operators	No. of Invalid Replicates
	Total	Lot 1	Lot 2	Lot 3				
A (Neg.)	91	26	38	27	35	7	14	3
B (High Neg.)	88	24	37	27	28	7	14	2
C (Equivocal)	78	27	44	8*	35	8	16	3
D (Low Pos.)	80	25	27	28	11	2	4	4
E (Mod. Pos.)	64	25	13	26	13	2	6	1
F (Pos.)	69	25	19	25	15	2	4	3

*Sufficient cartridges from reagent lot #3 were not available.

Results of the precision study are presented in Table 4.

Table 4: Summary of Precision Study Results

Panel Member	Mean (COI)		Repeatability (same device, same lot)	Between-device	Between-lot	Precision (same device, different lot)	Precision (different device, same lot)	Precision (different device, different lot)
A (Neg.)	0.425	SD	0.049	0.007	0.000	0.049	0.049	0.049
		%CV	11.5%	1.6%	0%	11.5%	11.6%	**11.6%**
B High Neg.)	0.648	SD	0.086	0.011	0.029	0.091	0.087	0.092
		%CV	13.3%	1.7%	4.5%	14.1%	13.4%	**14.2%**
C Equivocal)	1.016	SD	0.093	0.062	0.065	0.113	0.112	0.129
		%CV	9.1%	6.1%	6.4%	11.1%	11.0%	**12.7%**
D (Low Pos.)	1.727	SD	0.208	0.098	0.013	0.208	0.230	0.230
		%CV	12.0%	5.7%	0.8%	12.0%	13.3%	**13.3%**
E (Mod. Pos.)	3.809	SD	0.305	0.276	0.108	0.324	0.411	0.425
		%CV	8.0%	7.3%	2.8%	8.5%	10.8%	**11.2%**
F (Pos.)	8.996	SD	0.807	0.437	0.000	0.807	0.918	0.918
		%CV	9.0%	4.9%	0.0%	9.0%	10.2%	**10.2%**

Table 5 presents percent of invalid results and percents of negative, equivocal and positive among valid results for each sample.

Table 5: Percent of Invalid Results and Percents of Negative, Equivocal and Positive among Valid Results

Panel Member	Mean (COI)	Number of Replicates	Percent of Invalid	Percent of Negative among Valid	Percent of Equivocal among Valid	Percent of Positive among Valid
A (Neg.)	0.425	94	3.2% (3/94)	100% (91/91)		
B (High Neg.)	0.648	90	2.2% (2/90)	100% (88/88)		
C (Equivocal)	1.016	81	3.7% (3/81)	17.9% (14/78)	60.3% (47/78)	21.8% (17/78)
D (Low Pos.)	1.727	84	4.8% (4/84)			100% (80/80)
E (Mod. Pos.)	3.809	65	1.5% (1/65)			100% (64/64)
F (Pos.)	8.996	72	4.2% (3/72)			100% (69/69)

The results of the study demonstrate that the precision of the Theranos HSV-1 IgG Assay (including different TSPU devices, different lots of cartridges, and different operators) when performed in a CLIA Laboratory was in the range 10.2% to 14.2%.

Precision – CLIA Laboratory Model, Fingerstick Whole Blood

A study for estimating the precision of the Theranos HSV-1 IgG Assay for fingerstick whole blood samples in a CLIA Laboratory model was performed by testing a panel of 3 fingerstick plasma samples spanning the analytical range [high negative (P), equivocal (Q), moderate positive (R)]. The precision study was conducted at one site with thirty six (36) TSPU devices, three (3) lots of cartridges and nine (9) operators in total. The study duration was 4 days in total. Details of the study design for different samples are presented in Table 6 below.

Table 6: Design of Precision Study: Numbers of Replicates, Devices, Days and Operators

Panel Member	Valid Replicates				No. of Devices	No. of Days	No. of Operators	No. of Invalid Replicates
	Total	Lot 1	Lot 2	Lot 3				
P (High Neg.)	168	56	56	56	30	4	9	3*
Q (Equivocal)	168	56	56	56	29	4	9	2*
R (Mod. Pos.)	168	56	56	56	27	4	9	2*

*All invalid replicates were repeated

Results of the precision study are presented in Table 7.

Table 7: Summary of Precision Study Results

Panel Member	Mean (COI)		Repeatability (same device, same lot)	Between-device	Between-lot	Precision (same device, different lot)	Precision (different device, same lot)	Precision (different device, different lot)
P (High Neg.)	0.888	SD	0.083	0.006	0.050	0.096	0.083	0.097
		%CV	9.3%	0.7%	5.6%	10.9%	9.3%	**10.9%**
Q (Equivocal)	1.047	SD	0.094	0.025	0.069	0.117	0.098	0.119
		%CV	9.0%	2.4%	6.6%	11.1%	9.3%	**11.4%**
R (Mod. Pos.)	3.241	SD	0.342	0.122	0.157	0.377	0.363	0.396
		%CV	10.6%	3.8%	4.9%	11.6%	11.2%	**12.2%**

Table 8 presents percent of invalid results and percents of negative, equivocal and positive among valid results for each sample.

Table 8: Percents of Positive, Equivocal, Negative and Invalid Results

Panel Member	Mean (COI)	Number of Replicates	Percent of Invalid	Percent of Negative among Valid	Percent of Equivocal among Valid	Percent of Positive among Valid
P (High Neg.)	0.888	171	1.8% (3/171)	58.3% (98/168)	40.5% (68/168)	1.2% (2/168)
Q (Equivocal)	1.047	170	1.2% (2/170)	6.5% (11/168)	63.1% (106/168)	30.4% (51/168)
R (Mod. Pos.)	1.016	170	1.2% (2/170)			100% (168/168)

The results of the study demonstrate that precision of the Theranos HSV-1 IgG Assay (including different TSPU devices, different lots of cartridges, and different operators) when performed in a CLIA Laboratory was in the range from 10.9% to 12.2%.

Reproducibility

A study designed to process multiple fingerstick whole blood samples from individual subjects was performed to evaluate the reproducibility of the Theranos HSV-1 IgG Assay when used with Theranos Capillary Tubes and Nanotainer Tubes. The study was conducted at 3 collection sites with 10 subjects at each site. From each of 30 subjects, 9 Capillary Tubes and Nanotainer Tubes from 3 manufacturing lots (i.e. 3 Capillary Tubes and Nanotainer Tubes per lot) and 2 serum separator tubes (SSTs) were collected. Each subject had the following measurements:

- Each of the 9 Capillary Tubes and Nanotainer Tubes was tested. These data were used for evaluation of between-Capillary Tubes and Nanotainer Tubes imprecision, between-lot imprecision and total imprecision that includes between-Capillary Tubes and Nanotainer Tubes and between-lot imprecisions.
- One Nanotainer Tube (from one of the 3rd lot of Capillary Tubes and Nanotainer Tubes for each subject) was tested in duplicate via recovering a sample from one

Capillary Tubes and Nanotainer Tubes and transferring a sample to another Capillary Tubes and Nanotainer Tubes. These data were used for evaluation of within-Capillary Tubes and Nanotainer Tubes imprecision.

- Each of the 2 SSTs was tested. These data were used for evaluation of between-SST imprecision.

For samples with mean COI value at the baseline ≥0.5, percent differences were calculated and for samples with mean COI value at the baseline <0.5, differences were calculated. Table 9 summarizes the results of the reproducibility study broken down by collection site and by high or low COI subjects; the variability metrics are averaged across all subjects within the site.

Table 9: Summary of Results of the Reproducibility Study

Collection Site	Subjects	Capillary Tubes and Nanotainer Tubes				SST
		Within-Capillary Tubes and Nanotainer Tubes (%CV or SD)	Between-Capillary Tubes and Nanotainer Tubes (%CV or SD)	Between-Lot (%CV or SD)	Total (%CV or SD)	Between-SST (%CV or SD)
1	6 subjects with COI values 1.4 – 13.5	%CV=6.0%	%CV = 9.0%	%CV = 6.8%	%CV=12.6%	%CV=9.6%
	4 subjects with COI values 0.03-0.28	SD=0.008	SD = 0.015	SD = 0.016	SD = 0.024	SD=0.11
2	7 subjects with COI values 1.6 – 16.8	%CV=8.2%	%CV=9.2%	%CV=3.2%	%CV=10.8%	%CV=12.5%
	3 subjects with COI values 0.07-0.19	SD=0.009	SD=0.011	SD=0.008	SD=0.015	SD=0.019
3	5 subjects with COI values 4.5 – 14.3	%CV=8.2%	%CV=8.1%	%CV=6.0%	%CV=11%	%CV=12.4%
	5 subjects with COI values 0.02-0.32	SD=0.08	SD=0.019	SD=0.013	SD=0.025	SD=0.021
Combined	18 subjects with COI values 1.4-16.8	%CV=7.5%	%CV=8.8%	%CV=5.2%	%CV=11.4%	%CV=11.5%
	12 subjects with COI values 0.02-0.32	SD=0.008	SD=0.015	SD=0.013	SD=0.022	SD=0.017

- Within-Capillary Tubes and Nanotainer Tubes imprecision was %CV=7.5% for aggregated subjects with mean COI ≥ 0.5 and SD=0.008 for aggregated subjects with a mean COI < 0.5.

- Total imprecision including between-Capillary Tubes and Nanotainer Tubes and between-lot imprecisions was %CV= 11.4% for aggregated subjects with a mean COI ≥ 0.5 and SD=0.022 for aggregated subjects with a mean COI < 0.5.

- Between-serum separator tubes imprecision was %CV=11.5% for aggregated subjects with a mean COI ≥ 0.5 and SD=0.017 for aggregated subjects with a mean COI < 0.5.

Analyte Stability

An analyte stability study was performed to characterize the stability of HSV-1 IgG in clinical matrices as measured by the Theranos HSV-1 IgG Assay under different sample storage conditions and time periods. A summary of analyte storage conditions and durations for different sample types and matrices claimed for the Theranos HSV-1 IgG Assay is presented in Table 10.

Table 10: Summary of Analyte Storage Conditions and Durations

Condition	Venous Serum	Venous K2-EDTA Plasma	Fingerstick K2-EDTA Plasma	Fingerstick K2-EDTA Whole Blood
Stored at 2-8°C	48 hr	48 hr	48 hr	48 hr
Stored at room temperature (20-25°C)	6 hr	6 hr	6 hr	6 hr
Stored at -20°C	1 week	1 week	1 week	N/A
Freeze/thaw cycles	3	3	3	N/A

Within 2 hours after collection, one aliquot of each sample type or matrix was tested with the Theranos HSV-1 IgG Assay in duplicate, to establish the value at baseline. The samples were stored in Nanotainer Tubes under the appropriate conditions. Comparison of an average of two replicates at the predetermined time points with the average of two replicates at baseline was performed. For samples with a mean COI value at the baseline ≥0.5, percent differences were calculated and for samples with a mean COI value at the baseline <0.5, differences were calculated.

Acceptance criteria were as follows: i) a difference averaged over all samples with baseline mean COI value ≥0.5 must be less than ±10% and a difference averaged over all samples with baseline COI mean <0.5 must be less than 0.02 and ii) for each sample, an observed difference must be less than 15% for the samples with baseline mean COI value ≥0.5 and must be less than 0.08 for the samples with baseline mean COI value <0.5 (the range of differences expected if there is no effect of storage on the HSV-1 IgG analyte). The results are summarized in Table 11.

Table 11: Summary of Mean Absolute Difference Measures for all Storage Conditions and Sample Types or Matrices

	Sample Type and Matrix	Samples with a Baseline COI < 0.5		Samples with a Baseline COI > 0.5	
		Difference averaged over all samples	The largest observed difference among samples	Percent difference averaged over all samples	The largest observed percent difference among samples
Stored at 2-8C, 48 hrs	Venous serum	0.006	0.006	1.0%	13.6%
	Venous K2-EDTA plasma	-0.007	-0.007	2.3%	13.3%
	Fingerstick K2-EDTA plasma from whole blood	0.003	0.003	-0.4%	13.9%
Stored at -20, 1 week	Venous serum	0.008	0.015	0.8%	13.3%
	Venous K2-EDTA plasma	0.003	0.005	-1.0%	12.7%
	Fingerstick K2-EDTA plasma from whole blood	0.001	0.008	1.8%	-13.9%
Freeze thaw cycles, n=3	Venous serum	0.007	0.021	-0.1%	13.6%
	Venous K2-EDTA plasma	0.021	0.037	-1.7%	-13.4%
	Fingerstick K2-EDTA plasma from whole blood	0.006	0.022	-1.0%7	13.6%
Stored at room temp, 6 hrs	Venous serum	-0.001	-0.011	-3.2%	-11.9%
	Venous K2-EDTA plasma	0.002	0.022	0.1%	13.7%
	Fingerstick K2-EDTA plasma from whole blood	-0.004	-0.026	1.1%	13.9%

Interfering Substances

A study was designed and performed (in accordance with CLSI EP07-A2) to evaluate the performance of the Theranos HSV-1 IgG Assay in the presence of potentially interfering substances to assess the impact of these endogenous substances and commonly used drugs on the performance of the Theranos HSV-1 IgG Assay. Interferents were tested with three serum samples (negative (mean COI 0.024), high negative (mean COI 0.77) and low positive (mean COI 1.52)) that were contrived by using a high positive sample and diluting it with pooled negative serum. Samples were spiked with the interferent at levels shown in Table 12. Each serum pool was tested in duplicate.

For the low positive and the high negative pools, the acceptance criteria were a mean recovery within +/- 20% of the value of the unspiked sample (i.e., in the absence of the potential interferent or drug). All low positive and high negative samples showed a signal change of less than 15% for all interfering substances. All positive samples remained positive and all negative samples remained negative upon spiking of drug or other interferents. For the negative pool, the acceptance criterion was a deviation of less than 0.02 COI. All negative samples showed a mean deviation of ≤0.02 COI, except Intralipid. Intralipid spikes did not show any effect on recovery for near cut-off samples, high negative and low positive samples.

Table 12: Summary of Interfering Substances Studies: Endogenous Interferents and Drug Interferents

		Negative Pool		High Negative Pool		Low Positive Pool	
Interferent	**Level**	**Mean COI**	**ΔCOI**	**Mean COI**	**% Recovery**	**Mean COI**	**% Recovery**
Hemoglobin	1000 mg/dL	0.025	0.00	0.69	90	1.71	113
Bilirubin	20 mg/dL	0.024	0.00	0.68	88	1.61	106
Intralipid	2000 mg/dL	0.053	0.03	0.81	105	1.60	105
Acetylcysteine	150 mg/L	0.019	-0.004	0.68	88	1.40	92
Ampicillin-Na	1000 mg/L	0.025	0.001	0.76	99	1.44	95
Ascorbic acid	300 mg/L	0.027	0.003	0.75	97	1.67	110
Ca-Dobesilate	200 mg/L	0.027	0.004	0.70	91	1.51	99
Cyclosporine	5 mg/L	0.031	0.008	0.74	97	1.53	101
Cefoxitin	2500 mg/L	0.027	0.003	0.74	97	1.52	100
Heparin	5000U	0.020	-0.003	0.80	103	1.52	100

		Negative Pool		High Negative Pool		Low Positive Pool	
Interferent	**Level**	**Mean COI**	**ΔCOI**	**Mean COI**	**% Recovery**	**Mean COI**	**% Recovery**
Levodopa	20 mg/L	0.030	0.006	0.68	88	1.42	94
Methyldopa+1.5h20	20 mg/L	0.024	0.000	0.74	97	1.37	90
Metronidazole	200 mg/L	0.039	0.016	0.74	96	1.38	91
Phenylbutazone	400 mg/L	0.021	-0.002	0.74	96	1.42	94
Doxycycline	50 mg/L	0.024	0.000	0.71	92	1.35	89
Acetylsalicylic acid	1000 mg/L	0.026	0.002	0.75	97	1.37	90
Rifampicin	60 mg/L	0.014	-0.009	0.69	90	1.35	89
Acetaminophen	200 mg/L	0.034	0.010	0.64	83	1.68	111
Control		0.024	0.000	0.77	100	1.52	100

Cross-reactivity

A study was performed to evaluate the performance of the Theranos HSV-1 IgG Assay in the presence of IgG antibodies against twenty-one (21) infectious agents defined as potential cross-reactants in the FDA guidance on HSV serological assays. Banked serum samples confirmed positive for IgG against the infectious agents of interest were acquired from commercial vendors. At least three (3) samples, independently confirmed as positive for that agent and negative for HSV-1 IgG on the reference method, were tested on the Theranos HSV-1 IgG Assay in order to rule out cross-reactivity of the Theranos HSV-1 IgG Assay with IgG against a potential cross reactant. The results of this study are displayed in Table 13.

Table 13: Summary of Cross-reactivity Study on Theranos HSV-1 IgG Assay

Organism/Condition	No.	Reference HSV-1 Assay	Theranos HSV-1 Positive	Theranos HSV-1 Negative	Theranos HSV-1 Equivocal
Epstein Barr Virus (IgG)	6	Negative	0	6	0
Epstein Barr Virus (IgM)	1	Negative	0	1	0
HPV	4	Negative	0	4	0
Rubella (IgG)	13	Negative	0	13	0
HSV-2 (IgG)	40	Negative	0	40	0
HAMA samples	4	Negative	0	4	0
Treponema pallidum	8	Negative	0	7	1*
Rheumatoid Factor (RF)	8	Negative	1**	7	0
Anti-nuclear antibody (ANA)	8	Negative	0	8	0
Sjogren's Syndrome	3	Negative	0	3	0
CMV (IgG)	5	Negative	0	5	0
CMV (IgM)	2	Negative	0	2	0
Chlamydia trachomatis (IgG)	10	Negative	0	10	0
HCV (IgG)	3	Negative	0	3	0
HBsAg	3	Negative	0	3	0
VZV IgG	5	Negative	0	5	0
Measles IgG	5	Negative	0	5	0
HIV-1 (IgG)	4	Negative	0	4	0
Toxoplasma IgG	4	Negative	0	4	0
Candida albicans Ag	3	Negative	0	3	0
Systemic Lupus	3	Negative	0	3	0

*Systematic cross-reactivity ruled out (7/8 samples in same category tested negative)

**Confirmed as positive upon retest by Theranos HSV-1 assay; systematic cross-reactivity ruled out (7/8 samples in same category tested negative)

Assay Cut-off

A study was performed to establish the cut-off and the limits of the equivocal zone for the Theranos HSV-1 IgG Assay using 192 serum samples. Then 120 independent serum samples were analyzed to validate the established cut-off. The calibrators were assigned COI values based on the established assay cut-off, the cut-off for positive results a COI of 1.1 and cut-off for negative results a COI of 0.9. The results of the cut-off validation study are displayed in Table 14 below.

Table 14: Performance of Selected Cut-off on Independent Sample Set

Agreement Classification	Percent Agreement	95% Confidence Interval
NPA	96.0% (47/49)	86.3-98.9
PPA	97.1% (69/71)	90.3-99.2

Fingerstick Plasma – CLIA Laboratory Model

To demonstrate the performance of the Theranos HSV-1 IgG Assay for fingerstick whole blood samples collected at 3 Theranos Patient Service Centers (TPSCs) and processed at the CLIA-certified laboratory.

At each site, fingerstick whole blood samples were collected into a pair of Theranos Capillary Tubes and Nanotainer Tubes, and venous samples were collected into serum tubes from each of 20, 16 and 25 adult subjects at three collection sites.

Samples were shipped refrigerated to the Theranos CLIA-certified laboratory in Palo Alto, CA. Upon receipt, fingerstick whole blood samples in the Nanotainer Tubes were centrifuged at 1200g for 5 minutes. Plasma was extracted and processed and analyzed on the Theranos System. All samples were processed or frozen as plasma within 48 hours of draw.

A summary of the performance information is shown in Table 15.

Table 15: Summary of Method Comparison for Samples Collected at 3 Theranos Patient Service Centers

		Reference Result	
		POS	NEG
Theranos Result	POS	38	0
	NEG	1	22

	Point Estimate	95% Confidence Interval
Sensitivity	97.4% (38/39)	86.8 – 99.6
Specificity	100% (22/22)	85.1 – 100

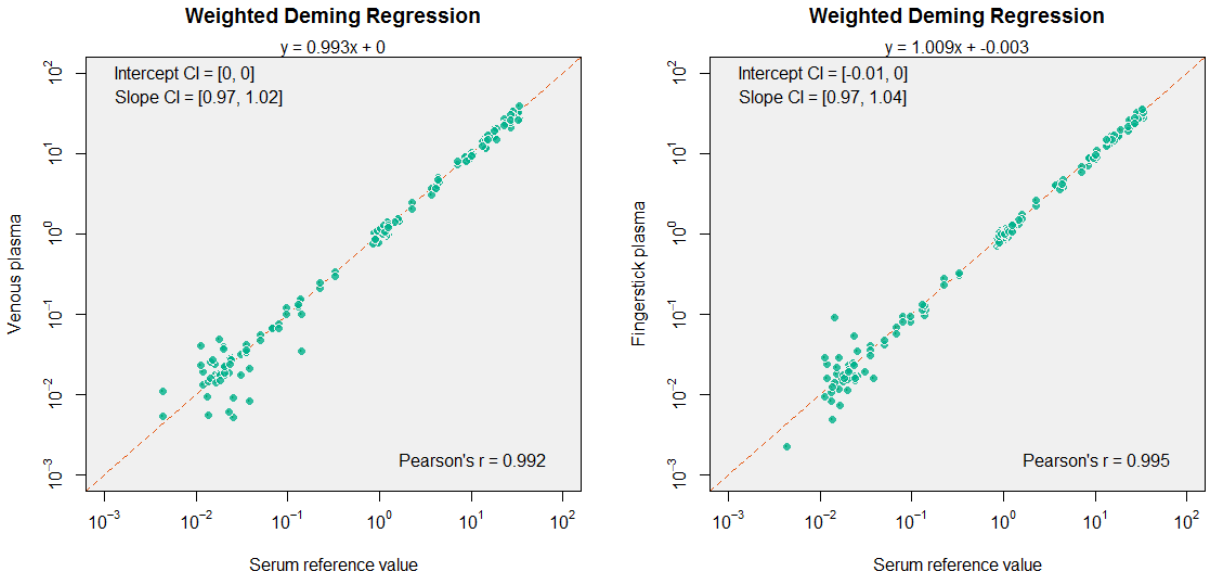
Matrix Comparison

The effect of anticoagulants and different sample types (fingerstick and venous) on the performance of the Theranos HSV-1 IgG Assay was determined by comparing matched venous serum, venous K2-EDTA plasma, and fingerstick K2-EDTA plasma samples from 70 donors. Forty-three matched sample sets were contrived to have analyte values close to the cut-off. The acceptance criterion was a recovery of positive plasma samples within ± 20% of the corresponding serum reference value (serum drawn into primary tubes without gel). For negative samples, the acceptance criteria was a difference of <= 0.02 COI from the corresponding serum value. All anticoagulant–treated plasma samples met this criterion. Weighted Deming regression was performed. The slope and an intercept of the regression line and their 95% confidence intervals along with correlation coefficients are shown in Table 16 and a graphical depiction is shown in Figure 1.

Table 16: Summary of Weighted Deming Regression Analysis Performed on Matrix Equivalency Data for Venous Plasma and Fingerstick Plasma Samples

Sample Type/Matrix	Correlation coefficient	Slope	95% confidence interval on slope	Intercept	95% confidence interval on intercept
Venous plasma	0.992	0.993	[0.967, 1.019]	0.000	[-0.003, 0.003]
Fingerstick plasma	0.995	1.009	[0.973, 1.044]	-0.003	[-0.006, -0.001]

Figure 1: Regression Analysis for Matrix Comparison Study



Expected Values

The Theranos HSV-1 IgG Assay was used to evaluate the prevalence of HSV-1 IgG antibodies in individuals for whom an HSV-1 IgG test was ordered by a physician including pregnant women. The study population for the Theranos HSV-1 IgG Assay consisted of a total of 558 subjects, with 260 sexually active adults and 298 individuals identified as pregnant women. The result for 1 out of the 558 subjects is not reported, as indicated in Table 17 (1 subject), giving a total of 557 subjects. The data for the intended use population (557 specimens) have been summarized according to age group in decades, gender, number of reactive results, number of equivocal results, and number of non-reactive results. The data for the intended use population have been summarized in Table 17 (259 specimens from sexually active adult subjects) and Table 18 (298 specimens from pregnant subjects).

Table 17: Expected Results for Theranos HSV-1 IgG Assay in Sexually Active Adult Subjects

Age Range	Gender	Reactive	Equivocal	Non-Reactive
		N/Total (%)	N/Total (%)	N/Total (%)
16 to 19	Male	0/0 (0)	0/0 (0)	0/0 (0)
16 to 19	Female	1/4 (25)	0/4 (0)	3/4 (75)
20 to 29	Male	8/18 (44.4)	1/18 (5.6)	9/18 (50)
20 to 29	Female	29/73 (39.7)	0/73 (0)	44/73 (60.3)
30 to 39	Male	5/10 (50)	0/10 (0)	5/10 (50)
30 to 39	Female	33/62 (53.2)	0/62 (0)	29/62 (46.8)
40 to 49	Male	5/10 (50)	0/10 (0)	5/10 (50)
40 to 49	Female	16/27 (59.3)	0/27 (0)	11/27 (40.7)
50 to 59	Male	17/20 (85)	0/20 (0)	3/20 (15)
50 to 59	Female	9/11 (81.8)	0/11 (0)	2/11 (18.2)
60 to 69	Male	5/6 (83.3)	0/6 (0)	1/6 (16.7)
60 to 69	Female	5/10 (50)	1/10 (10)	4/10 (40)
70 to 79	Male	3/4 (75)	0/4 (0)	1/4 (25)
70 to 79	Female	1/3 (33.3)	0/3 (0)	2/3 (66.7)
80 to 89	Male	0/0 (0)	0/0 (0)	0/0 (0)
80 to 89	Female	1/1 (100)	0/1 (0)	0/1 (0)
Total*		138/259 (53.3)	2/259 (0.8)	119/259 (45.9)

*1 sample not reported since age information was not available

Table 18: Expected Results for Theranos HSV-1 IgG Assay in Pregnant Subjects

Age Range	Gender	Reactive	Equivocal	Non-Reactive
		N/Total (%)	N/Total (%)	N/Total (%)
18 to 19	Female	13/13 (100)	0/13 (0)	0/13 (0)
20 to 29	Female	114/175 (65.1)	1/175 (0.6)	60/175 (34.3)
30 to 39	Female	61/104 (58.7)	0/104 (0)	43/104 (41.3)
40 to 49	Female	5/6 (83.3)	0/6 (0)	1/6 (16.7)
Total		193/298 (65)	1/298 (0.3)	104/298 (35)

The hypothetical positive and negative predictive values (PPV, NPV) for the two intended use populations are shown in Table 19. The calculations are based on the specificity and sensitivity values for the Theranos HSV-1 IgG Assay determined in the clinical study;

1. Specificity of 97.4% and Sensitivity of 95.1% in sexually active adults
2. Specificity of 95.2% and Sensitivity of 97.4% in pregnant women

Table 19: Hypothetical Predictive Values

Prevalence (%)	Sexually Active Adults		Pregnant Women	
	PPV (%)	NPV (%)	PPV (%)	NPV (%)
50	93.8	92.6	92.1	91.7
45	93.2	93.2	91.3	92.4
40	92.4	93.8	90.3	93.0
35	91.4	94.2	89.1	93.5
30	90.1	94.6	87.5	94.0
25	88.3	94.9	85.3	94.3
20	85.8	95.2	82.3	94.7
15	82.0	95.5	77.7	95.0
10	75.2	95.7	69.9	95.2
5	60.2	96.0	53.8	95.5

Clinical Performance in the Intended Use Populations (CLIA Laboratory Model)

A clinical study was conducted to characterize the performance of the Theranos HSV-1 IgG Assay in the Theranos CLIA-certified Laboratory in comparison to the FOCUS HerpeSelect Immunoblot (as the reference method for performance analysis).

Prospectively collected, archived venous serum samples collected from pregnant women and sexually active adults (18 years and older) who had a prescription for a HSV-1 IgG test. Samples were obtained from multiple specimen sources covering 10 US states and Mexico.

The equivocal results on the Focus HerpeSelect Immunoblot (that repeatedly tested equivocal) were resolved using a validated western blot reference test (University of Washington, Seattle) as per the instructions of the package insert for the reference method. Ten samples from the sexually active adult sub-population tested initially equivocal on the Focus HerpeSelect Immunoblot and were resolved by the University of Washington western blot as 2 negatives and 7 positives. One sample was not resolved. There were no samples in the sexually active adult sub-population that returned an invalid result.

In the pregnant women sub-population, 8 samples tested initially equivocal on the Focus HerpeSelect immunoblot. Of these, 4 samples could not be resolved by the University of Washington western blot due to insufficient volume availability. Of the remaining 4, 1 (one) were resolved as negative and 3 as positive. There were 3 samples that returned an invalid result on the Theranos HSV-1 IgG test. These samples were rerun and resulted in

valid results included in the analysis. The clinical performance results are summarized in Tables 20 and 21.

Table 20: Summary of Theranos HSV-1 IgG Assay Performance in Sexually Active Adult Population

		Reference Method			
		Positive	Equivocal	Negative	Total
Theranos HSV-1 IgG Assay	Positive	137	0	2	139
	Equivocal	1	0	1	2
	Negative	5	1	113	119
	Total	143	1	116	***260***

	Point Estimate	95% Confidence Interval
Sensitivity	95.1% (137/144)	90.3-97.6
Specificity	97.4% (113/116)	92.7-99.1

Table 21: Summary of Theranos HSV-1 IgG Assay Performance in Pregnant Women Population

		Reference Method			
		Positive	Equivocal	Negative	Total
Theranos HSV-1 IgG Assay	Positive	188	1	4	193
	Equivocal	0	1	0	1
	Negative	2	2	100	104
	Total	190	4	104	***298***

	Point Estimate	95% Confidence Interval
Sensitivity	97.9% (188/192)	94.8-99.2
Specificity	95.2% (100/105)	89.3-98.0

CDC Panel Testing

The objective of this study was to demonstrate agreement of the Theranos HSV-1 IgG Assay with the CDC panel. A panel of well characterized serum samples (n=100) was obtained from the U.S. Centers for Disease Control and Prevention (CDC). The CDC sample panel was tested with the HSV-1 IgG Assay and the results obtained by Theranos were sent to the CDC for confirmation. The panel consisted of 54 positives and 46 negatives. The Theranos HSV-1 IgG Assay demonstrated 100% agreement with the results provided by the CDC.

Low Prevalence Population

Serum samples were collected from a low prevalence population: Individuals who are not sexually active, and without a recent or current sexually transmitted disease (Hepatitis, Syphilis, HIV, HPV, Trichomonas, Chlamydia, Gonorrhoeae) as determined in an interview. Performance of the assay on this population is summarized in Table 22. The Samples were obtained from multiple specimen sources covering 10 US states and Mexico.

Table 22: Summary of Theranos HSV-1 IgG Assay Performance with Low Prevalence Population

		Reference Method			
		Positive	Equivocal	Negative	Total
Theranos HSV-1 IgG Assay	Positive	32	0	0	32
	Equivocal	0	0	0	0
	Negative	0	1	49	50
	Total	32	1	49	***82***

	Point Estimate	95% Confidence Interval
Sensitivity	97.0% (32/33)	84.7-99.5
Specificity	100% (49/49)	92.7-100

CONCLUSIONS

The results of the analytical and clinical performance studies submitted in this premarket notification are complete and demonstrate that the Theranos HSV-1 IgG Assay meets the established specifications necessary for consistent performance during intended clinical use. The results support a decision that the Theranos Herpes Simplex Virus-1 (HSV-1) IgG Assay is substantially equivalent to the predicate.