September 6, 2024

Beckman Coulter, Inc
Brenda Eifert
Staff Regulatory Affairs
1000 Lake Hazeltine Drive
Chaska, Minnesota 55318

Re: K241427
Trade/Device Name: Access Syphilis
Regulation Number: 21 CFR 866.3830
Regulation Name: Treponema Pallidum Treponemal Test Reagents
Regulatory Class: Class II
Product Code: LIP
Dated: May 17, 2024
Received: May 20, 2024

Dear Brenda Eifert:

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 (the 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. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database available at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm identifies combination product submissions. 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.

Additional information about changes that may require a new premarket notification are provided in the FDA guidance documents entitled "Deciding When to Submit a 510(k) for a Change to an Existing Device"

(https://www.fda.gov/media/99812/download) and "Deciding When to Submit a 510(k) for a Software Change to an Existing Device" (https://www.fda.gov/media/99785/download).

Your device is also subject to, among other requirements, the Quality System (QS) regulation (21 CFR Part 820), which includes, but is not limited to, 21 CFR 820.30, Design controls; 21 CFR 820.90, Nonconforming product; and 21 CFR 820.100, Corrective and preventive action. Please note that regardless of whether a change requires premarket review, the QS regulation requires device manufacturers to review and approve changes to device design and production (21 CFR 820.30 and 21 CFR 820.70) and document changes and approvals in the device master record (21 CFR 820.181).

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801 and Part 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR Part 803) for devices or postmarketing safety reporting (21 CFR Part 4, Subpart B) for combination products (see https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR Part 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR Parts 1000-1050.

All medical devices, including Class I and unclassified devices and combination product device constituent parts are required to be in compliance with the final Unique Device Identification System rule ("UDI Rule"). The UDI Rule requires, among other things, that a device bear a unique device identifier (UDI) on its label and package (21 CFR 801.20(a)) unless an exception or alternative applies (21 CFR 801.20(b)) and that the dates on the device label be formatted in accordance with 21 CFR 801.18. The UDI Rule (21 CFR 830.300(a) and 830.320(b)) also requires that certain information be submitted to the Global Unique Device Identification Database (GUDID) (21 CFR Part 830 Subpart E). For additional information on these requirements, please see the UDI System webpage at https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/unique-device-identification-system-udi-system.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance) and CDRH Learn (https://www.fda.gov/training-and-continuing-education/cdrh-learn). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/contact-us-division-industry-and-consumer-education-dice) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Himani Bisht -S

Himani Bisht, Ph.D.
Assistant Director
Viral Respiratory and HPV Branch
Division of Microbiology Devices
OHT7: Office of In Vitro Diagnostics
and Radiological Health
Office of Product Evaluation and Quality
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Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: 07/31/2026
See PRA Statement below.

Submission Number *(if known)*

K241427

Device Name

Access Syphilis

Indications for Use *(Describe)*

The Access Syphilis assay is a paramagnetic particle, chemiluminescent immunoassay for the qualitative detection of total antibodies to Treponema pallidum in human serum and plasma using the Access Immunoassay Systems. It is intended to be used as an aid in the diagnosis of syphilis or in conjunction with a nontreponemal laboratory test and clinical findings to aid in the diagnosis of syphilis infection. The Access Syphilis assay is not intended for blood and tissue donor screening.

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.

510(k) Summary

This summary of 510(k) safety and effectiveness information is being submitted in accordance with the requirements of SMDA 1990 and 21 CFR 807.92.

510(k) Number: K241427 **Date Prepared:** September 6, 2024

Submitter Name and Address:
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Trade Name: Access Syphilis
Common Name: *Treponema pallidum* treponemal test reagents
Classification Regulation: 21 CFR 866.3830
Classification Product Code*:* LIP

Predicate Device:
Abbott ARCHITECT™ Syphilis TP, 8D06

Device Description

The Access Syphilis assay is a two-step enzyme immunoassay. A sample is added to a reaction vessel with buffer, paramagnetic particles coated with recombinant *Treponema pallidum* antigens Tp17 and Tp47, and biotinylated Treponema Tp17 & Tp47 antigens. After incubation in a reaction vessel, materials bound to the solid phase are held in a magnetic field while unbound materials are washed away. Alkaline phosphatase conjugates are added, and the conjugates bind to the immunoglobulin captured on the particles. A chemiluminescent substrate is added to the vessel and light generated by the reaction is measured with a luminometer. The light production is proportional to the amount of *Treponema pallidum* antibodies in the sample. The light quantity measured for a sample allows a determination of the presence of the analyte by comparison with a cut-off value defined during the assay calibration on the instrument.

The Access Syphilis reagents are provided in liquid ready-to-use format designed for optimal performance on the Beckman Coulter Access Immunoassay Systems. Each reagent kit contains two reagent packs.

Intended Use

The Access Syphilis assay is a paramagnetic particle, chemiluminescent immunoassay for the qualitative detection of total antibodies to *Treponema pallidum* in human serum and plasma using the Access Immunoassay Systems. It is intended to be used as an aid in the diagnosis of syphilis or in conjunction with a non-treponemal laboratory test and clinical findings to aid in the diagnosis of syphilis infection. The Access Syphilis assay is not intended for blood and tissue donor screening.

Comparison Table

Features / Characteristics	**Candidate Device** Access Syphilis	**Predicate Device (K153730)** ARCHITECT Syphilis
Reagent Intended Use **and Clinical Indications**	**Access Immunoassay Systems IFU:** The Access Syphilis assay is a paramagnetic particle, chemiluminescent immunoassay for the qualitative detection of total antibodies to *Treponema pallidum* in human serum and plasma using the Access Immunoassay Systems. **It is intended to be used as an aid in the diagnosis of syphilis or in conjunction with a nontreponemal laboratory test and clinical findings to aid in the diagnosis of syphilis infection.** The Access Syphilis assay is not intended for blood and tissue donor screening.	The ARCHITECT Syphilis TP assay is a chemiluminescent microparticle immunoassay (CMIA) for the qualitative detection of antibodies (IgG and IgM) directed against *Treponema pallidum* (TP) in human serum and plasma. **The ARCHITECT Syphilis TP assay is intended to be used as an initial diagnostic test or in conjunction with a nontreponemal laboratory test and clinical findings to aid in the diagnosis of syphilis infection.** Warning: The ARCHITECT Syphilis TP assay is not intended for use in screening blood, plasma, or tissue donors. The effectiveness of the ARCHITECT Syphilis TP assay for use in screening blood, plasma, or tissue donors has not been established.
Environment of Use	Health Care Providers requesting samples to be tested by clinical laboratory technicians	Same
Operating Principle	Chemiluminescent microparticle immunoassay (CMIA)	Same
Antigen sources	Recombinant *Treponema pallidum* antigens Tp17 and Tp47, and biotinylated Treponema Tp17 & Tp47 antigens	Recombinant TP antigens: TpN15, TpN17 and TpN47 (obtained in *E.coli*)
Assay Type	Two-step sandwich enzyme immunoassay	Same
Detection Method	Automated, Chemiluminescence	Same
Reagent format	Liquid, ready to use	Same
Sample Type	Serum and Plasma	Same

Features / Characteristics	**Candidate Device** Access Syphilis	**Predicate Device (K153730)** ARCHITECT Syphilis
Compatible Anticoagulants	<u>Human Serum:</u> Serum and serum separator tube <u>Human Plasma:</u> Lithium Heparin Lithium Heparin separator tube Dipotassium (K_2) EDTA Tripotassium (K_3) EDTA Sodium Citrate Acid Citrate Dextrose (ACD) Citrate Phosphate Dextrose (CPD) Citrate Phosphate Dextrose with Adenine (CPDA)	<u>Human Serum:</u> Serum and serum separator tube <u>Human Plasma:</u> Dipotassium EDTA Tripotassium EDTA Lithium heparin plasma separator Lithium heparin Sodium heparin
Sample Volume	~45 µL	30 µL
Instrumentation	Access Immunoassay Systems: ▪ Access 2 Immunoassay System ▪ DxI 9000 Access Immunoassay Analyzer	ARCHITECT iSystem
Test Result Reporting	Reactive, Non-reactive and S/CO	Reactive, Non-reactive and S/CO
Time to Result	▪ Access 2 Immunoassay System ~30 minutes ▪ DxI 9000 Access Immunoassay Analyzer ~22 minutes	~ 29 minutes
Reagent Storage and Stability	Unopened at 2 to 10°C up to stated expiration date	Unopened at 2 to 8°C up to stated expiration date
Reagent On-board Stability	56 Days	30 days

Summary of Studies – Access 2 Immunoassay System

Imprecision

The assay was designed to have within-laboratory imprecision as listed below:

- ≤ 0.10 SD at concentrations of < 1.00 S/CO
- ≤ 10.0% CV at concentrations ≥ 1.00 S/CO

The imprecision of the Access Syphilis assay on the Access 2 Immunoassay Systems was evaluated in a study based on CLSI EP05-A3 guidance.

The within-laboratory intermediate precision study included two test runs per day over 20 test days. A four-member panel of serum (S1-S4) samples and the Access Syphilis QC were assayed in each run (in duplicate). Three lots of Access Syphilis reagent and calibrator were tested on an Access 2 Immunoassay Analyzer for the study. The results are presented below:

			Between Lot		Between Day		Between Run		Within Run		Overall	
Sample	**N**	**Mean** (S/CO)	**SD** (S/CO)	**%CV**	**SD** (S/CO)	**%CV**	**SD** (S/CO)	**%CV**	**SD** (S/CO)	**%CV**	**SD** (S/CO)	**%CV**
QC1	240	0.107	0.029	N/A	0.009	N/A	0.007	N/A	0.007	N/A	0.032	N/A
QC2	240	1.704	0.083	4.9%	0.057	3.4%	0.074	4.3%	0.048	2.8%	0.134	7.9%
S1 (Low Negative)	240	0.064	0.004	N/A	0.003	N/A	0.004	N/A	0.003	N/A	0.007	N/A
S2 (High Negative)	240	0.708	0.018	2.6%	0.023	3.2%	0.022	3.2%	0.017	2.5%	0.041	5.8%
S3 (Low Positive)	240	1.819	0.116	6.4%	0.061	3.4%	0.051	2.8%	0.039	2.2%	0.146	8.0%
S4 (Positive)	240	6.721	0.491	7.3%	0.216	3.2%	0.203	3.0%	0.179	2.7%	0.601	8.9%

Note: %CV are not meaningful when dose approaches zero. Results are noted as N/A.

Between-Lot Precision

A six-member panel, including serum samples (S1-S4) and two assay controls, were assayed at three clinical sites, using three lots of Access Syphilis reagent to obtain between-lot precision. Each panel member was assayed in replicates of four, twice a day over 5 days. The results are summarized in the following table.

			Within Reagent Pack Lot		Between Reagent Pack Lot		Total	
Sample	**N**	**Mean (S/CO)**	**SD (S/CO)**	**%CV**	**SD (S/CO)**	**%CV**	**SD (S/CO)**	**%CV**
QC1	360	0.10	0.01	N/A	0.02	N/A	0.03	N/A
QC2	360	1.56	0.09	5.5	0.01	0.9	0.09	5.5
S1 (Low Negative)	360	0.06	0.01	N/A	0.00	N/A	0.01	N/A
S2 (High Negative)	360	0.75	0.03	4.3	0.01	1.9	0.03	4.7
S3 (Low Positive)	360	1.89	0.09	4.5	0.06	3.1	0.10	5.5
S4 (Positive)	360	7.19	0.30	4.2	0.25	3.5	0.39	5.4

Note: %CV are not meaningful when dose approaches zero. Results are noted as N/A.

Reproducibility

A 5-day between lab reproducibility study was performed on the Access 2 Immunoassay Systems based on CLSI EP05- A3 guidance. A six-member panel, including serum samples (S1-S4) and two assay controls, were assayed at three clinical sites, using three lots of Access Syphilis reagent on three instruments. Each panel member was assayed in replicates of four at two separate times per day. The results are summarized in the following table.

			Repeatability (Within Run)		Between Run		Between Day		Between Lot		Between Site		Reproducibility	
Sample	**N**	**Mean** (S/CO)	**SD** (S/CO)	**%CV**	**SD** (S/CO)	**%CV**	**SD** (S/CO)	**%CV**	**SD** (S/CO)	**%CV**	**SD** (S/CO)	**%CV**	**SD** (S/CO)	**%CV**
QC1	360	0.10	0.004	N/A	0.005	N/A	0.006	N/A	0.025	N/A	0.005	N/A	0.027	N/A
QC2	360	1.56	0.043	2.8	0.058	3.7	0.016	1.0	0.010	0.6	0.054	3.4%	0.092	5.9
S1 (Low Negative)	360	0.06	0.003	N/A	0.003	N/A	0.003	N/A	0.005	N/A	0.005	N/A	0.009	N/A
S2 (High Negative)	360	0.75	0.019	2.6	0.018	2.4	0.018	2.5	0.013	1.8	0.005	0.6%	0.035	4.7
S3 (Low Positive)	360	1.89	0.042	2.2	0.065	3.5	0.037	2.0	0.058	3.1	0.000	N/A	0.104	5.5
S4 (Positive)	360	7.19	0.223	3.1	0.197	2.7	0.000	N/A	0.247	3.4	0.068	0.9%	0.393	5.5

Note: %CV are not meaningful when dose approaches zero. Results are noted as N/A.

INTERFERING SUBSTANCES

The Access Syphilis assay was evaluated for interference consistent with CLSI document EP07 3rd Edition. Testing was performed using two nonreactive (one low negative and one high negative) and two reactive (one low positive and one positive) samples. Of the endogenous compounds tested, none were found to cause interference at the highest test concentrations indicated in the following table.

Potential Interferent	Highest Concentration
Hemoglobin	1,000 mg/dL
Total Protein	15 g/dL
Bilirubin - conjugated	40 mg/dL
Bilirubin - unconjugated	40 mg/dL
Triolein	36 g/L
Biotin	0.351 mg/dL
Gamma globulin	47.5 g/L*

*Interference was noted at a concentration of 60 g/L. A dose effect study was conducted, with no interference observed ≤47.5 g/L.

The following pharmaceutical substances were also evaluated and no interference with the assay was observed: acetylsalicylic acid (aspirin), acetaminophen (paracetamol), ibuprofen, azithromycin, ceftriaxone sodium, doxycycline hyclate.

Cross Reactivity

Cross-reactivity was evaluated by testing samples for potentially cross-reacting conditions. No cross-reactivity was observed. The results are summarized in the following table.

Category	Number of Samples Tested	Number of Reactive Samples	Number of Nonreactive Samples
Pregnant multipara	**14**	0	14
Hemodialysis patients	**10**	0	10
Transplant patients	**10**	0	10
Rheumatoid Factor (RF)	**10**	0	10
Human Anti-mouse Antibody (HAMA)	**10**	0	10
Anti-Nuclear Antibody (ANA)	**10**	0	10
Lyme Disease (*Borrelia garinii, Borrelia afzelii & Borrelia burgdorferi* s.s.)	**10**	0	10
Toxoplasma gondii IgG	**5**	0	5
Toxoplasma gondii IgM	**5**	0	5
Epstein Barr Virus (EBV) IgG	**10**	0	10
Epstein Barr Virus (EBV) IgM	**10**	0	10
Leptospirosis	**10**	0	10
Systemic Lupus Erythemateous (SLE)	**10**	0	10
Hepatitis A Virus (HAV) Total Ab	**5**	0	5
Hepatitis A Virus (HAV) IgM	**5**	0	5
Hepatitis B Virus (HBV) - HBs Ag positive	**10**	0	10
Hepatitis B Virus (HBV) -anti-HBs positive	**22**	0	22
Hepatitis B Virus (HBV) - HBc IgM positive	**9**	0	9
Hepatitis B Virus (HBV) - Anti HBc total positive	**20**	0	20
Hepatitis C Virus (HCV)	**10**	0	10
HTLV-1	**10**	0	10
HTLV-2	**13**	0	13
Human Immunodeficiency Virus (HIV)-1	**8**	0	8
Human Immunodeficiency Virus (HIV)-2	**9**	0	9
Herpes Simplex Virus (HSV) 1& 2 IgM	**15**	0	15
Herpes Simplex Virus (HSV) 1 IgG	**10**	0	10
Herpes Simplex Virus (HSV) 2 IgG	**2**	0	2
Cytomegalovirus (CMV) IgG	**5**	0	5
Cytomegalovirus (CMV) IgM	**5**	0	5
Rubella IgG	**5**	0	5
Rubella IgM	**10**	0	10
Anti-*Escherichia coli* (E.*coli*)	**10**	0	10
Multiple myeloma	**10**	0	10
Flu vaccinated patients	**10**	0	10
Anti-Phospholipid	**10**	0	10
TOTAL	**337**	**0**	**337**

Clinical Performance Evaluation – Access 2 Immunoassay System

A total of 1,104 prospectively collected specimens from the intended use population were tested using the Access Syphilis assay. 704 (63.8%) were female and 400 (36.2%) were male, with an age range of 12 to > 89 years. The Access Syphilis assay was reactive in 214 (19.4%) of specimens collected from the intended use population.

Distribution of the Access Syphilis Reactive and Nonreactive results in the intended use population by age and gender

Age Range (Years)	Gender	Total	Access Syphilis Assay	
			Reactive N (%)	Nonreactive N (%)
12-20	Male	7	0 (0.0)	7 (100.0)
	Female	48	2 (4.2)	46 (95.8)
21-30	Male	44	9 (20.4)	35 (79.6)
	Female	256	8 (3.1)	248 (96.9)
31-40	Male	72	36 (50.0)	36 (50.0)
	Female	211	12 (5.7)	199 (94.3)
41-50	Male	87	38 (43.7)	49 (56.3)
	Female	68	9 (13.2)	59 (86.8)
51-60	Male	123	54 (43.9)	69 (56.1)
	Female	68	17 (25.0)	51 (75.0)
61-70	Male	54	16 (29.6)	38 (70.4)
	Female	38	10 (26.3)	28 (73.7)
71-89*	Male	13	2 (15.4)	11 (84.6)
	Female	15	1 (6.7)	14 (93.3)
Total		**1,104**	**214 (19.4)**	**890 (80.6)**

* NOTE: One (1) subject was > 89 years

Clinical Performance

A multicenter study was conducted to evaluate the clinical performance of the Access Syphilis assay. A total of 1,910 specimens were included in this study with 1,104 prospectively collected specimens from the intended use population, 402 retrospective specimens from patients, 204 prospectively collected specimens from apparently healthy individuals, 150 retrospective specimens from patients with medically diagnosed syphilis, and 50 retrospective specimens from individuals at high-risk of sexually transmitted disease.

The specimens were tested at three sites in a randomized and blinded fashion (all cohorts), using the Access Syphilis assay, and a final comparator result was obtained using a composite testing algorithm consisting of the following FDA-approved assays: the predicate treponemal immunoassay, a nontreponemal assay (RPR – Rapid Plasma Reagin), and a second treponemal assay (TPPA - Treponema Pallidum Particle Agglutination).

Clinical Performance in Intended Use Population

A total of 1,104 specimens from the intended use population were prospectively collected and tested with Access Syphilis and the composite testing algorithm described above. The study included specimens from 399 patients sent for syphilis testing, 405 pregnant women and 300 HIV positive patients.

Summary of the Serological Profile for all Prospectively Collected Specimens from the Intended Use Population

Predicate Treponemal Immunoassay	RPR	TPPA	Final Comparator Result	Access Syphilis Result	N
-	-	NA	-	-	878
-	+	-	-	-	5
-	+	+	+	-	0
+	-	-	-	-	7
+	-	+	+	-	0
+	+	NA	+	-	0
-	+	INC	-	-	0
+	+	NA	+	+	79
+	-	+	+	+	104
+	-	-	-	+	12
-	+	+	+	+	0
-	+	-	-	+	0
-	-	-	-	+	13
-	-	+	-	+	5
+	-	INC	+	+	1
				Total	**1,104**

+ = Reactive; - = Nonreactive; NA = not performed; INC = Inconclusive

The overall positive percent agreement was 100% (184/184) with a 95% confidence interval of 98.0 to 100% and the overall negative percent agreement was 96.7% (890/920) with a 95% confidence interval of 95.4 to 97.7%

Percent Agreement for Intended Use Subpopulations

Subpopulation	Positive Percent Agreement		Negative Percent Agreement	
	n/N	% (95% CI)	n/N	% (95% CI)
Routine Syphilis Testing	60/60	100 (94.0 - 100)	338/339[1]	99.7 (98.4 – 100)
Pregnant Women	6/6	100 (61.0 - 100)	398/399	99.8 (98.6 - 100)
HIV Positive Patients	118/118	100 (96.9 - 100)	154/182[2]	84.6 (78.7 - 89.1)
Total	**184/184**	**100 (98.0 - 100)**	**890/920**	**96.7 (95.4 - 97.7)**

[1] One (1) specimen from the routine syphilis testing cohort was reactive by an FDA-cleared treponemal immunoassay and nonreactive by RPR and TPPA.

[2]Twenty-five (25) out of twenty-eight (28) discordants were found to be reactive using an additional FDA-cleared electrochemiluminescent immunoassay. Eleven (11) of these were also reactive by the predicate treponemal immunoassay.

Clinical Performance in Retrospective Specimens

A cohort of 402 retrospective specimens were included in the study, of which 22 were from pregnant females.

Summary of the Serological Profile for Retrospective Specimens

Predicate Treponemal Immunoassay	RPR	TPPA	Final Comparator Result	Access Syphilis Result	N
-	-	NA	-	-	1
-	+	-	-	-	0
-	+	+	+	-	0
+	-	-	-	-	0
+	-	+	+	-	0
+	+	NA	+	-	0
-	+	INC	-	-	0
+	+	NA	+	+	324
+	-	+	+	+	74
+	-	-	-	+	3
-	+	+	+	+	0
-	+	-	-	+	0
-	-	-	-	+	0
-	-	+	-	+	0
+	-	INC	+	+	0
				Total	**402**

+ = Reactive; - = Nonreactive; NA = not performed; INC = Inconclusive

Comparison between the Access Syphilis Results and the Final Comparator Results in Retrospective Specimens

Retrospective Specimens		Final Comparator Result		
		Reactive	Nonreactive	Total
Access Syphilis Result	Reactive	398	3 [1]	401
	Nonreactive	0	1	1
	Total	398	4	402

[1]Three (3) specimens were reactive by treponemal immunoassay and nonreactive by RPR and TPPA

The positive percent agreement was 100% (398/398) with a 95% confidence interval of 99.0 to 100% and the negative percent agreement was 25.0% (1/4) with a 95% confidence interval of 4.6 to 69.9%.

Clinical Performance in Apparently Healthy Individuals

Of the total 1,910 specimens in the study, 204 were prospectively collected from apparently healthy individuals. Results of the Access Syphilis assay are shown below:

Apparently Healthy Individuals	Access Syphilis Result	
	Reactive (%)	Nonreactive (%)
	18 (8.8)	186 (91.2)

Clinical Performance in Medically Diagnosed Patients

A total of 150 retrospective specimens from patients with medically diagnosed syphilis (primary, secondary, and latent stages) were included in the study. Results of the Access Syphilis assay are shown in the following table:

Syphilis Stage	Treatment Status	N	Access Syphilis	
			Reactive	Nonreactive
Primary	Untreated	49	49	0
	Treated	27	26	1[1]
Secondary	Untreated	13	13	0
	Treated	23	23	0
Latent	Untreated	13	7	6[1]
	Treated	25	25	0

[1] These seven (7) specimens also tested nonreactive with an FDA-cleared treponemal immunoassay.

Clinical Performance in Pregnant Females

A total of 427 pregnant female specimens were included in the study, with 405 prospectively collected and 22 retrospectively collected specimens. **Percent Agreement Between Access Syphilis and the Final Comparator Result by Trimester**

Trimester	N	Positive Percent Agreement % (x/n)	95% Confidence Interval (%)	Negative Percent Agreement % (x/n)	95% Confidence Interval (%)
Prospectively Collected					
First Trimester	60	100 (1/1)	20.7 – 100	100 (59/59)	93.9 -100
Second Trimester	38	100 (1/1)	20.7 – 100	100 (37/37)	90.6 -100
Third Trimester	307	100 (4/4)	51.0 – 100	99.7 (302/303)	98.2 – 99.9
Unknown Trimester	0	NA	NA	NA	NA
Total	**405**	**100 (6/6)**	**61.0 – 100**	**99.8 (398/399)**	**98.6 – 100**
Retrospective Specimens					
First Trimester	6	100 (6/6)	61.0 – 100	NA (0/0)	NA
Second Trimester	9	100 (9/9)	70.1 – 100	NA (0/0)	NA
Third Trimester	6	100 (5/5)	56.6 – 100	100 (1/1)	20.7 – 100
Unknown Trimester	1	NA (0/0)	20.7 – 100	0 (0/1)	0 – 79.4
Total	**22**	**100 (20/20)**	**83.9 – 100**	**50.0 (1/2)**	**9.5 – 90.6**

NA – Not applicable

Clinical Performance in High-Risk Individuals

Of the total 1,910 specimens in the study, 50 retrospective specimens were from individuals at high-risk of sexually transmitted disease.

Comparison Between the Access Syphilis Results and the Final Comparator Results in High-Risk Individuals

High-Risk Individuals		Final Comparator Result		
		Reactive	Nonreactive	Total
Access Syphilis Result	Reactive	20	6[1]	26
	Nonreactive	0	24	24
	Total	20	30	50

[1] One (1) specimen was reactive by treponemal immunoassay and nonreactive by RPR and TPPA

The percent agreement was 100% (20/20) with a 95% confidence interval of 83.9 to 100% and the negative percent agreement was 80.0% (24/30) with a 95% confidence interval of 62.7 to 90.5%.

Summary of Studies – DxI 9000 Immunoassay Analyzer

Imprecision

The assay was designed to have within-laboratory imprecision as listed below:

- ≤ 0.10 SD at concentrations of < 1.00 S/CO
- ≤ 10.0% CV at concentrations ≥ 1.00 S/CO

The imprecision of the Access Syphilis assay on the DxI 9000 Access Immunoassay Analyzer was evaluated in a study based on CLSI EP05-A3 guidance.

The within-laboratory intermediate precision study included two test runs per day over 20 test days. A four-member panel of serum (S1-S4) samples and the Access Syphilis QC were assayed in each run (in duplicate). Three lots of Access Syphilis reagent and calibrator were tested on two DxI 9000 Access Immunoassay Analyzers for the study, with each lot tested on one instrument. The results are presented below:

			Between Lot & Instrument		**Between Day**		**Between Run**		**Within Run**		**Overall**	
Sample	**N**	**Mean** (S/CO)	**SD** (S/CO)	**%CV**	**SD** (S/CO)	**%CV**	**SD** (S/CO)	**%CV**	**SD** (S/CO)	**%CV**	**SD** (S/CO)	**%CV**
QC1	238	0.166	0.064	N/A	0.007	N/A	0.007	N/A	0.008	N/A	0.065	N/A
QC2	238	1.786	0.082	4.6%	0.059	3.3%	0.088	4.9%	0.041	2.3%	0.140	7.8%
S1 (Low Negative)	240	0.078	0.018	N/A	0.003	N/A	0.003	N/A	0.005	N/A	0.019	N/A
S2 (High Negative)	239	0.779	0.065	8.4%	0.021	2.8%	0.023	3.0%	0.019	2.4%	0.075	9.6%
S3 (Low Positive)	240	1.994	0.078	3.9%	0.048	2.4%	0.072	3.6%	0.046	2.3%	0.125	6.3%
S4 (Positive)	240	7.598	0.294	3.9%	0.241	3.2%	0.240	3.2%	0.163	2.1%	0.478	6.3%

Note: %CV are not meaningful when dose approaches zero. Results are noted as N/A.

Between-Lot Precision

A six-member panel, including serum samples (S1-S4) and two assay controls, were assayed at three clinical sites, using three lots of Access Syphilis reagent to obtain between-lot precision. Each panel member was assayed in replicates of four, twice a day over 5 days. The results are summarized in the following table.

			Within Reagent Pack Lot		Between Reagent Pack Lot		Total	
Sample	**N**	**Mean** (S/CO)	**SD** (S/CO)	**%CV**	**SD** (S/CO)	**%CV**	**SD** (S/CO)	**%CV**
QC1	360	0.10	0.013	N/A	0.033	N/A	0.035	N/A
QC2	360	1.59	0.087	5.5	0.005	0.3	0.087	5.5
S1 (Low Negative)	360	0.05	0.007	N/A	0.007	N/A	0.010	N/A
S2 (High Negative)	360	0.75	0.045	6.0	0.019	2.6	0.048	6.5
S3 (Low Positive)	360	1.94	0.109	5.6	0.056	2.9	0.122	6.3
S4 (Positive)	360	7.48	0.537	7.2	0.303	4.0	0.616	8.2

Note: %CV are not meaningful when dose approaches zero. Results are noted as N/A.

Reproducibility

A 5-day between lab reproducibility study was performed on the DxI 9000 Access Immunoassay analyzer based on CLSI EP05-A3 guidance[14]. A six-member panel, including serum samples (S1-S4) and two assay controls, were assayed at three clinical sites, using three lots of Access Syphilis reagent on three instruments. Each panel member was assayed in replicates of four at two separate times per day. The results are summarized in the following table.

			Repeatability (Within Run)		Between Run		Between Day		Between Lot		Between Site		Reproducibility	
Sample	**N**	**Mean** (S/CO)	**SD** (S/CO)	**%CV**	**SD** (S/CO)	**%CV**	**SD** (S/CO)	**%CV**	**SD** (S/CO)	**%CV**	**SD** (S/CO)	**%CV**	**SD** (S/CO)	**%CV**
QC1	360	0.10	0.005	N/A	0.003	N/A	0.009	N/A	0.033	N/A	0.010	N/A	0.036	N/A
QC2	360	1.59	0.037	2.3	0.050	3.2	0.059	3.7	0.000	N/A	0.019	1.2	0.088	5.5
S1 (Low Negative)	360	0.05	0.003	N/A	0.001	N/A	0.004	N/A	0.007	N/A	0.005	N/A	0.010	N/A
S2 (High Negative)	360	0.75	0.017	2.3	0.018	2.4	0.029	3.8	0.018	2.4	0.030	4.0	0.052	6.9
S3 (Low Positive)	360	1.94	0.044	2.3	0.060	3.1	0.070	3.6	0.053	2.7	0.052	2.7	0.126	6.5
S4 (Positive)	360	7.48	0.271	3.6	0.271	3.6	0.213	2.8	0.297	4.0	0.387	5.2	0.655	8.8

Note: %CV are not meaningful when dose approaches zero. Results are noted as N/A.

Interfering Substances

The Access Syphilis assay was evaluated for interference consistent with CLSI document EP07 3rd Edition. Testing was performed using two nonreactive (one low negative and one high negative) and two reactive (one low positive and one positive) samples. Of the endogenous compounds tested, none were found to cause interference at the highest test concentrations indicated in the following table.

Potential Interferent	Highest Concentration
Hemoglobin	1,000 mg/dL
Total Protein	15 g/dL
Bilirubin - conjugated	40 mg/dL
Bilirubin - unconjugated	40 mg/dL
Triolein	36 g/L
Biotin	0.351 mg/dL
Gamma globulin	47.5 g/L*

*Interference was noted at a concentration of 60 g/L. A dose effect study was conducted, with no interference observed ≤47.5 g/L.

The following pharmaceutical substances were also evaluated and no interference with the assay was observed: acetylsalicylic acid (aspirin), acetaminophen (paracetamol), ibuprofen, azithromycin, ceftriaxone sodium, doxycycline hyclate.

Cross Reactivity

Cross-reactivity was evaluated by testing samples for potentially cross-reacting conditions. No cross-reactivity was observed. The results are summarized in the following table.

Category	Number of Samples Tested	Number of Reactive Samples	Number of Nonreactive Samples
Pregnant multipara	**14**	0	14
Hemodialysis patients	**10**	0	10
Transplant patients	**10**	0	10
Rheumatoid Factor (RF)	**10**	0	10
Human Anti-mouse Antibody (HAMA)	**10**	0	10
Anti-Nuclear Antibody (ANA)	**10**	0	10
Lyme Disease (*Borrelia garinii, Borrelia afzelii & Borrelia burgdorferi* s.s.)	**10**	0	10
Toxoplasma gondii IgG	**5**	0	5
Toxoplasma gondii IgM	**5**	0	5
Epstein Barr Virus (EBV) IgG	**10**	0	10
Epstein Barr Virus (EBV) IgM	**10**	0	10
Leptospirosis	**10**	0	10
Systemic Lupus Erythemateous (SLE)	**10**	0	10
Hepatitis A Virus (HAV) Total Ab	**5**	0	5
Hepatitis A Virus (HAV) IgM	**5**	0	5
Hepatitis B Virus (HBV) - HBs Ag positive	**10**	0	10
Hepatitis B Virus (HBV) -anti-HBs positive	**22**	0	22
Hepatitis B Virus (HBV) - HBc IgM positive	**9**	0	9
Hepatitis B Virus (HBV) - Anti HBc total positive	**20**	0	20
Hepatitis C Virus (HCV)	**10**	0	10
HTLV-1	**10**	0	10
HTLV-2	**13**	0	13
Human Immunodeficiency Virus (HIV)-1	**8**	0	8
Human Immunodeficiency Virus (HIV)-2	**9**	0	9
Herpes Simplex Virus (HSV) 1& 2 IgM	**15**	0	15
Herpes Simplex Virus (HSV) 1 IgG	**10**	0	10
Herpes Simplex Virus (HSV) 2 IgG	**2**	0	2
Cytomegalovirus (CMV) IgG	**5**	0	5
Cytomegalovirus (CMV) IgM	**5**	0	5
Rubella IgG	**5**	0	5
Rubella IgM	**10**	0	10
Anti-*Escherichia coli* (E.*coli*)	**10**	0	10
Multiple myeloma	**10**	0	10
Flu vaccinated patients	**10**	0	10
Anti-Phospholipid	**10**	0	10
TOTAL	**337**	**0**	**337**

Clinical Performance Evaluation – Dxl 9000 Immunoassay Analyzer

A total of 1,104 prospectively collected specimens from the intended use population were tested using the Access Syphilis assay. 704 (63.8%) were female and 400 (36.2%) were male, with an age range of 12 to > 89 years. The Access Syphilis assay was reactive in 214 (19.4%) of specimens collected from the intended use population.

Distribution of the Access Syphilis Reactive and Nonreactive Results in the Intended Use Population by Age and Gender

Age Range (Years)	Gender	Total	Access Syphilis Assay	
			Reactive N (%)	Nonreactive N (%)
12-20	Male	7	0 (0.0)	7 (100.0)
	Female	48	2 (4.2)	46 (95.8)
21-30	Male	44	9 (20.4)	35 (79.6)
	Female	256	8 (3.1)	248 (96.9)
31-40	Male	72	36 (50.0)	36 (50.0)
	Female	211	12 (5.7)	199 (94.3)
41-50	Male	87	38 (43.7)	49 (56.3)
	Female	68	9 (13.2)	59 (86.8)
51-60	Male	123	54 (43.9)	69 (56.1)
	Female	68	17 (25.0)	51 (75.0)
61-70	Male	54	16 (29.6)	38 (70.4)
	Female	38	10 (26.3)	28 (73.7)
71-89*	Male	13	2 (15.4)	11 (84.6)
	Female	15	1 (6.7)	14 (93.3)
Total		**1,104**	**214 (19.4)**	**890 (80.6)**

* NOTE: One (1) subject was > 89 years

Clinical Performance

A multicenter study was conducted to evaluate the clinical performance of the Access Syphilis assay. A total of 1,910 specimens were included in this study with 1,104 prospectively collected specimens from the intended use population, 402 retrospective specimens from patients , 204 prospectively collected specimens from apparently healthy individuals, 150 retrospective specimens from patients with medically diagnosed syphilis, and 50 retrospective specimens from individuals at high-risk of sexually transmitted disease.

The specimens were tested at three sites in a randomized and blinded fashion (all cohorts), using the Access Syphilis assay, and a final comparator result was obtained using a composite testing algorithm consisting of the following FDA-approved assays: the predicate treponemal immunoassay, a nontreponemal assay (RPR – Rapid Plasma Reagin), and a second treponemal assay (TPPA - Treponema Pallidum Particle Agglutination).

Clinical Performance in Intended Use Population

A total of 1,104 specimens from the intended use population were prospectively collected and tested with Access Syphilis and the composite testing algorithm described above. The study included specimens from 399 patients sent for syphilis testing, 405 pregnant women and 300 HIV positive patients.

Summary of the Serological Profile for all Prospectively Collected Specimens from the Intended Use Population

Predicate Treponemal Immunoassay	RPR	TPPA	Final Comparator Result	Access Syphilis Result	N
-	-	NA	-	-	878
-	+	-	-	-	5
-	+	+	+	-	0
+	-	-	-	-	7
+	-	+	+	-	0
+	+	NA	+	-	0
-	+	INC	-	-	0
+	+	NA	+	+	79
+	-	+	+	+	104
+	-	-	-	+	12
-	+	+	+	+	0
-	+	-	-	+	0
-	-	-	-	+	13
-	-	+	-	+	5
+	-	INC	+	+	1
				Total	**1,104**

+ = Reactive; - = Nonreactive; NA = not performed; INC = Inconclusive

The overall positive percent agreement was 100% (184/184) with a 95% confidence interval of 98.0 to 100% and the overall negative percent agreement was 96.7% (890/920) with a 95% confidence interval of 95.4 to 97.7%.

Percent Agreement for Intended Use Subpopulations

Subpopulation	Positive Percent Agreement		Negative Percent Agreement	
	n/N	% (95% CI)	n/N	% (95% CI)
Routine Syphilis Testing	60/60	100 (94.0 - 100)	338/339[1]	99.7 (98.4 – 100)
Pregnant Women	6/6	100 (61.0 - 100)	398/399	99.8 (98.6 - 100)
HIV Positive Patients	118/118	100 (96.9 - 100)	154/182[2]	84.6 (78.7 - 89.1)
Total	**184/184**	**100 (98.0 - 100)**	**890/920**	**96.7 (95.4 - 97.7)**

[1] One (1) specimen from the routine syphilis testing cohort was reactive by an FDA-cleared treponemal immunoassay and nonreactive by RPR and TPPA.

[2]Twenty-five (25) out of twenty-eight (28) discordants were found to be reactive using an additional FDA-cleared electrochemiluminescent immunoassay. Eleven (11) of these were also reactive by the predicate treponemal immunoassay.

Clinical Performance in Retrospective Specimens

A cohort of 402 retrospective specimens from patients were included in the study, of which 22 were from pregnant females.

Summary of the Serological Profile for Retrospective Specimens

Predicate Treponemal Immunoassay	RPR	TPPA	Final Comparator Result	Access Syphilis Result	N
-	-	NA	-	-	1
-	+	-	-	-	0
-	+	+	+	-	0
+	-	-	-	-	0
+	-	+	+	-	0
+	+	NA	+	-	0
-	+	INC	-	-	0
+	+	NA	+	+	324
+	-	+	+	+	74
+	-	-	-	+	3
-	+	+	+	+	0
-	+	-	-	+	0
-	-	-	-	+	0
-	-	+	-	+	0
+	-	INC	+	+	0
				Total I	**402**

+ = Reactive; - = Nonreactive; NA = not performed; INC = Inconclusive

Comparison Between the Access Syphilis Results and the Final Comparator Results in Retrospective Specimens

Retrospective Specimens		Final Comparator Result		
		Reactive	Nonreactive	Total
Access Syphilis Result	Reactive	398	3 1	401
	Nonreactive	0	1	1
	Total	398	4	402

[1]Three (3) specimens were reactive by treponemal immunoassay and nonreactive by RPR and TPPA

The positive percent agreement was 100% (398/398) with a 95% confidence interval of 99.0 to 100% and the negative percent agreement was 25.0% (1/4) with a 95% confidence interval of 4.6 to 69.9%.

Clinical Performance in Apparently Healthy Individuals

Of the total 1,910 specimens in the study, 204 were prospectively collected from apparently healthy individuals. Results of the Access Syphilis assay are shown below:

Apparently Healthy Individuals	Access Syphilis Result	
	Reactive (%)	Nonreactive (%)
	18 (8.8)	186 (91.2)

Clinical Performance in Medically Diagnosed Patients

A total of 150 retrospective specimens from patients with medically diagnosed syphilis (primary, secondary, and latent stages) were included in the study. Results of the Access Syphilis assay are shown in the following table:

Syphilis Stage	Treatment Status	N	Access Syphilis	
			Reactive	Nonreactive
Primary	Untreated	49	49	0
	Treated	27	26	1[1]
Secondary	Untreated	13	13	0
	Treated	23	23	0
Latent	Untreated	13	7	6[1]
	Treated	25	25	0

[1] These seven (7) specimens also tested nonreactive with an FDA-cleared treponemal immunoassay.

Clinical Performance in Pregnant Females

A total of 427 pregnant female specimens were included in the study, with 405 prospectively collected and 22 retrospective specimens.

Percent Agreement Between Access Syphilis and the Final Comparator Result by Trimester

Trimester	N	Positive Percent Agreement % (x/n)	95% Confidence Interval (%)	Negative Percent Agreement % (x/n)	95% Confidence Interval (%)
Prospectively Collected					
First Trimester	60	100 (1/1)	20.7 – 100	100 (59/59)	93.9 -100
Second Trimester	38	100 (1/1)	20.7 – 100	100 (37/37)	90.6 -100
Third Trimester	307	100 (4/4)	51.0 – 100	99.7 (302/303)	98.2 – 99.9
Unknown Trimester	0	NA	NA	NA	NA
Total	**405**	**100 (6/6)**	**61.0 – 100**	**99.8 (398/399)**	**98.6 – 100**
Retrospective Specimens					
First Trimester	6	100 (6/6)	61.0 – 100	NA (0/0)	NA
Second Trimester	9	100 (9/9)	70.1 – 100	NA (0/0)	NA
Third Trimester	6	100 (5/5)	56.6 – 100	100 (1/1)	20.7 – 100
Unknown Trimester	1	NA (0/0)	20.7 – 100	0 (0/1)	0 – 79.4
Total	**22**	**100 (20/20)**	**83.9 – 100**	**50.0 (1/2)**	**9.5 – 90.6**

NA – Not applicable

Clinical Performance in High-Risk Individuals

Of the total 1,910 specimens in the study, 50 retrospective specimens were from individuals at high-risk of sexually transmitted disease.

Comparison Between the Access Syphilis Results and the Final Comparator Results in High-Risk Individuals

High-Risk Individuals		Final Comparator Result		
		Reactive	Nonreactive	Total
Access Syphilis Result	Reactive	20	6 [1]	26
	Nonreactive	0	24	24
	Total	20	30	50

[1] One (1) specimen was reactive by treponemal immunoassay and nonreactive by RPR and TPPA

The positive percent agreement was 100% (20/20) with a 95% confidence interval of 83.9 to 100% and the negative percent agreement was 80.0% (24/30) with a 95% confidence interval of 62.7 to 90.5%.

Substantial Equivalence Comparison Conclusion

Beckman Coulter's Access Syphilis is substantially equivalent to the ARCHITECT Syphilis TP Reagent as demonstrated through the information and data provided in this submission. The performance and clinical testing presented in this submission provides evidence that the device is safe and effective for its intended use.