



June 15, 2016

Food and Drug Administration  
10903 New Hampshire Avenue  
Document Control Center – WO66-G609  
Silver Spring, MD 20993-0002

Abbott Laboratories Diagnostic Division  
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Re: K153730

Trade/Device Name: ARCHITECT Syphilis TP Reagent Kit, ARCHITECT Syphilis TP Calibrator, ARCHITECT Syphilis TP Controls  
Regulation Number: 21 CFR 866.3830  
Regulation Name: *Treponema pallidum* treponemal test reagents  
Regulatory Class: Class II  
Product Code: LIP, JIT, JJX  
Dated: May 20, 2016  
Received: May 23, 2016

Dear Dr. Joglekar:

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 regulation (21 CFR Part 801), 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" (21CFR 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,

**Steven R. Gitterman -S**

Uwe Scherf, M.Sc., Ph.D.

Director

Division of Microbiology Devices

Office of In Vitro Diagnostics and

Radiological Health

Center for Devices and Radiological Health

Enclosure

## Indications for Use

510(k) Number (if known)  
k153730

### Device Name

ARCHITECT Syphilis TP Reagent Kit  
ARCHITECT Syphilis TP Calibrator  
ARCHITECT Syphilis TP Controls

### Indications for Use (Describe)

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.

The ARCHITECT Syphilis TP Calibrator is for the calibration of the ARCHITECT iSystem when used for the qualitative detection of antibody to *Treponema pallidum* (TP) in human serum and plasma.

The ARCHITECT Syphilis TP Controls are for the estimation of test precision and the detection of systematic analytical deviations of the ARCHITECT iSystem when used for the qualitative detection of antibody to *Treponema pallidum* (TP) in human serum and plasma.

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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## Section 5: 510(k) Summary

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

### I. Applicant Name

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### II. Device Name

ARCHITECT Syphilis TP (8D06)

#### Reagents

Trade Name: ARCHITECT Syphilis TP Reagent Kit  
Device Classification: Class II  
Classification Name: *Treponema pallidum* treponemal test reagents  
Governing Regulation: 21 CFR § 866.3830  
Code: LIP

#### Calibrator

Trade Name: ARCHITECT Syphilis TP Calibrator  
Device Classification: Class II  
Classification Name: Calibrator  
Governing Regulation: 862.1150  
Code: JIT

## Controls

Trade Name: ARCHITECT Syphilis TP Controls  
Device Classification: Class I  
Classification Name: Control  
Governing Regulation: 862.1660  
Code: JJX

### **III. Predicate Device**

DiaSorin LIAISON Treponema assay (k061247)

### **IV. Description of Device**

#### Reagents

The ARCHITECT Syphilis TP reagent kit contains:

- **Microparticles:** (1 bottle x 6.6 mL per 100-test / 1 bottle x 27.0 mL per 500-test) TP (*E.coli*, recombinant) antigen coated microparticles in HEPES buffer with detergent. Minimum concentration: 0.08% solids. Preservatives: sodium azide and other antimicrobial agents.
- **Conjugate:** (1 bottle x 5.9 mL per 100-test / 1 bottle x 26.3 mL per 500-test). Murine anti-IgG/anti-IgM acridinium-labeled conjugate in MES buffer with protein (bovine) stabilizer. Minimum concentration: (anti-IgG) 26.6 ng/mL / (anti-IgM) 1.34 ng/mL. Preservatives: sodium azide and other antimicrobial agents.
- **Assay Diluent:** (1 bottle x 10.0 mL per 100-test / 1 bottle x 52.5 mL per 500-test). Syphilis TP Assay Diluent containing MES buffer with detergent. Preservatives: ProClin 950 and other antimicrobial agents.

#### Calibrator

The ARCHITECT Syphilis TP Calibrator contains:

- 1 Bottle (4.0 mL) of ARCHITECT Syphilis TP Calibrator. ARCHITECT Syphilis TP Calibrator is prepared in recalcified human plasma (inactivated); reactive for anti-TP. Preservatives: sodium azide and other antimicrobial agents.

The calibrator is referenced to an Abbott internal reference standard. This internal reference standard is manufactured by dilution of high titer positive plasma with HEPES buffer with nonreactive human plasma.

## Controls

The ARCHITECT Syphilis TP Controls contain:

- 1 Bottle (8.0 mL) Negative Control prepared in recalcified human plasma. Preservatives: sodium azide and other antimicrobial agents.
- 1 Bottle (8.0 mL) Positive Control prepared in recalcified human plasma. The Positive Control (inactivated) is reactive for anti-TP. Preservatives: sodium azide and other antimicrobial agents.

The controls are at the following proposed target syphilis TP concentrations and ranges:

<b>Control</b>	<b>Control Range S/CO</b>
Negative Control (Control -)	$\leq 0.40$
Positive Control (Control +)	1.25 - 3.75

## Biological Principles of the Procedure

The ARCHITECT Syphilis TP assay is a two-step immunoassay for the qualitative detection of antibodies (IgG and IgM) directed against TP in human serum or plasma using CMIA technology with flexible assay protocols, referred to as Chemiflex.

1. Sample, assay diluent, and recombinant TP antigen (TpN15, TpN17 and TpN47) coated microparticles are combined. Anti-TP antibodies present in the sample bind to the TP coated microparticles.
2. After washing, anti-human IgG and IgM acridinium-labeled conjugate is added to create a reaction mixture.
3. Following another wash cycle, Pre-Trigger and Trigger Solutions are added to the reaction mixture.
4. The resulting chemiluminescent reaction is measured as relative light units (RLUs). There is a direct relationship between the amount of anti-TP antibodies in the sample and the RLUs detected by the ARCHITECT iSystem optics.

The presence or absence of anti-TP antibodies in the specimen is determined by comparing the chemiluminescent signal in the reaction to the cutoff signal determined from an active calibration. If the chemiluminescent signal in the reaction is greater than or equal to the cutoff signal, the specimen is considered reactive for anti-TP antibodies.

## V. Intended Use of the Device

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.

## VI. Comparison of Technological Characteristics

The ARCHITECT Syphilis TP assay (candidate assay) utilizes a chemiluminescent microparticle immunoassay (CMIA) methodology for the quantitative *in vitro* determination of syphilis TP and is intended for use on the ARCHITECT iSystem.

The similarities and differences between the candidate assay and the predicate assay are presented in the tables starting on [page 5-5](#).

**Similarities**

<b>Characteristics</b>	<b>Candidate Device ARCHITECT Syphilis TP (List No. 8D06)</b>	<b>Predicate Device DiaSorin LIAISON<sup>†</sup> Treponema Assay (k061247)</b>
Intended Use and Indications for Use	The ARCHITECT Syphilis TP assay is a chemiluminescent microparticle immunoassay (CMIA) for the qualitative detection of antibodies (IgG and IgM) directed against <i>Treponema pallidum</i> (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.	The LIAISON Treponema Assay uses chemiluminescent immunoassay (CLIA) technology on the LIAISON Analyzer family for the qualitative determination of total antibodies directed against <i>Treponema pallidum</i> in human serum. The presence of antibodies to <i>Treponema pallidum</i> specific antigen, in conjunction with non-treponemal laboratory tests and clinical findings may aid in the diagnosis of syphilis infection.
Methodology	Chemiluminescent microparticle immunoassay (CMIA)	Sandwich chemiluminescence immunoassay (CLIA)
Cut-off Index	1.00 S/CO	Index value of 1.0
Standardization	The calibrator is referenced to an internal reference standard.	The calibrator concentrations are referenced to an in-house antibody preparation.
Controls	2 (Negative and Positive)	2 (Negative and Positive)

<sup>†</sup> DiaSorin LIAISON is the property of its respective owner.

**Differences**

<b>Characteristics</b>	<b>Candidate Device ARCHITECT Syphilis TP (List No. 8D06)</b>	<b>Predicate Device DiaSorin LIAISON Treponema Assay (k061247)</b>
Antigen Used	recombinant TP antigens: TpN15, TpN17 and TpN47 (obtained in <i>E.coli</i> )	DNA-Tp17 Recombinant antigen (obtained in <i>E. coli</i> )
Platform	ARCHITECT i2000SR System	DiaSorin LIAISON
Assay Protocol	2-step	1-step
Specimen Type	Human serum or plasma	Human serum
Equivocal Zone	No gray zone	Index value of 0.9 – 1.1
Components	<p><u>Microparticles</u> – TP (<i>E.coli</i>, recombinant) antigen coated microparticles in HEPES buffer with detergent. Minimum concentration: 0.08% solids. Preservatives: sodium azide and other antimicrobial agents.</p> <p><u>Conjugate</u> – Murine anti-IgG/anti-IgM acridinium-labeled conjugate in MES buffer with protein (bovine) stabilizer. Minimum concentration: (anti-IgG) 26.6 ng/mL / (anti-IgM) 1.34 ng/mL. Preservatives: sodium azide and other antimicrobial agents.</p> <p><u>Assay Diluent</u> – Syphilis TP Assay Diluent containing MES buffer with detergent. Preservatives: ProClin 950 and other antimicrobial agents.</p>	<p><u>Magnetic Particles</u> – Magnetic particles coated with Tp17 DNA recombinant protein (obtained in <i>E. coli</i>), BSA, phosphate buffer. Preservative: 0.099% Sodium Azide.</p> <p><u>Conjugate</u> – Tp17 DNA recombinant protein (obtained in <i>E. coli</i>) conjugated to an isoluminol derivative, BSA, phosphate buffer. Preservatives: ProClin 300, Gentamycin Sulfate.</p> <p><u>Specimen Diluent</u> – EDTA, phosphate buffer, bacterial proteins, an inert blue dye. Preservative: ProClin 300.</p>

**Differences**

<b>Characteristics</b>	<b>Candidate Device ARCHITECT Syphilis TP (List No. 8D06)</b>	<b>Predicate Device DiaSorin LIAISON Treponema Assay (k061247)</b>
Tube Types	Human serum: <ul style="list-style-type: none"> <li>• Serum</li> <li>• Serum separator</li> </ul> Human plasma: <ul style="list-style-type: none"> <li>• Dipotassium EDTA</li> <li>• Tripotassium EDTA</li> <li>• Lithium heparin plasma separator</li> <li>• Lithium heparin</li> <li>• Sodium heparin</li> </ul>	Serum
Calibrators	1 Positive Calibrator	2 Positive Calibrators
Calibration Storage	Maximum of 30 days	Maximum of 2 weeks

## VII. Summary of Nonclinical Performance

### Assay Cutoff

An internal study and an external clinical study were performed in order to select and validate the appropriate cutoff multiplier for the ARCHITECT Syphilis TP assay. The cutoff calculation is as follows:

$$\text{Cutoff (CO)} = \text{Calibrator Mean RLU}^{\dagger} \times 0.20$$

$$\text{S/CO} = \text{Sample RLU} / \text{Cutoff RLU}$$

Results < 1.00 S/CO are reported as nonreactive. Results  $\geq$  1.00 are reported as reactive.

### Precision

#### Within-Laboratory Precision

A study was performed based on guidance from Clinical and Laboratory Standards Institute (CLSI) document EP05-A2. Testing was conducted using 3 lots of ARCHITECT Syphilis TP Reagents, 2 lots of ARCHITECT Syphilis TP Calibrator, and 1 lot of ARCHITECT Syphilis TP Controls, and 2 instruments. Two controls and 4 serum panels were assayed in a minimum of 2 replicates (target of 3 replicates) at 2 separate times per day on 22 different days.

Sample	Instrument	Lot	N	Mean S/CO	Within-Run		Within-Laboratory <sup>a</sup> (Total)	
					SD	%CV	SD	%CV
Negative Control	1	1	130	0.04	0.002	4.3	0.002	4.9
		2	131	0.04	0.004	11.1	0.005	13.9
		3	131	0.04	0.004	11.7	0.005	13.8
	2	1	130	0.04	0.002	5.4	0.002	5.4
		2	130	0.04	0.005	14.3	0.005	14.7
		3	132	0.03	0.004	13.1	0.004	13.6
Positive Control	1	1	132	2.71	0.035	1.3	0.053	2.0
		2	132	2.68	0.034	1.3	0.058	2.2
		3	131	2.70	0.034	1.3	0.056	2.1
	2	1	132	2.66	0.048	1.8	0.060	2.3
		2	131	2.65	0.066	2.5	0.094	3.6
		3	131	2.66	0.048	1.8	0.069	2.6

<sup>†</sup> RLU = Relative Light Units

Sample	Instrument	Lot	N	Mean S/CO	Within-Run		Within-Laboratory <sup>a</sup> (Total)	
					SD	%CV	SD	%CV
Nonreactive Panel	1	1	132	0.08	0.004	4.3	0.005	5.6
		2	132	0.08	0.004	5.2	0.004	5.5
		3	132	0.08	0.004	5.3	0.005	6.9
	2	1	131	0.08	0.003	4.4	0.004	4.7
		2	132	0.08	0.005	6.3	0.005	7.0
		3	131	0.07	0.004	5.8	0.004	6.1
High Nonreactive Panel	1	1	132	0.57	0.010	1.8	0.013	2.3
		2	132	0.56	0.010	1.8	0.013	2.3
		3	132	0.56	0.010	1.9	0.014	2.4
	2	1	132	0.54	0.012	2.2	0.013	2.4
		2	131	0.54	0.013	2.4	0.017	3.2
		3	131	0.53	0.013	2.4	0.015	2.8
Low Reactive Panel	1	1	132	1.28	0.017	1.3	0.023	1.8
		2	132	1.27	0.018	1.5	0.026	2.1
		3	131	1.26	0.020	1.6	0.026	2.1
	2	1	130	1.24	0.025	2.0	0.030	2.4
		2	132	1.23	0.024	2.0	0.031	2.5
		3	132	1.22	0.024	2.0	0.031	2.5
High Reactive Panel	1	1	132	3.62	0.056	1.5	0.063	1.7
		2	132	3.60	0.052	1.5	0.063	1.8
		3	132	3.59	0.043	1.2	0.059	1.6
	2	1	132	3.55	0.065	1.8	0.079	2.2
		2	132	3.53	0.146	4.1	0.157	4.4
		3	132	3.54	0.064	1.8	0.082	2.3

<sup>a</sup> If no result was obtained for one of the target three replicates for a panel or control within a run, the lost replicate was not retested.

## Interference

A study was performed based on guidance from CLSI EP07-A2. Potentially interfering substances were evaluated to determine whether S/CO values were affected when using the ARCHITECT Syphilis TP assay. Samples containing the potential interferents were prepared at 2 levels of syphilis (approximately 0.80 S/CO and 1.20 S/CO). The samples were assayed, and the S/CO values of the spiked samples were compared to the reference samples. The ARCHITECT Syphilis TP assay is not susceptible to interference effects from the following interferents at the interferent levels listed in the table below.

Interferent	Interferent Level
Conjugated Bilirubin	≤ 20 mg/dL
Unconjugated Bilirubin	≤ 20 mg/dL
Cholesterol	≤ 500 mg/dL

<b>Interferent</b>	<b>Interferent Level</b>
Gamma Globulin	≤ 6 g/dL
Hemoglobin	≤ 500 mg/dL
Triglycerides	≤ 3000 mg/dL
Total Protein	≤ 12 g/dL

### **Analytical Specificity**

The ARCHITECT Syphilis TP assay was evaluated for potential cross-reactivity from specimens from individuals with medical conditions and other disease states unrelated to a syphilis infection.

Six specimens reactive in ARCHITECT Syphilis TP and a treponemal chemiluminescent immunoassay (TP-CLIA) were also either positive (marked by <sup>a</sup> in table below) or indeterminate (marked by <sup>d</sup> in table below) by confirmation testing. Confirmed reactive results were not unexpected because the specimens had been obtained from vendors based on the required disease condition and documentation of prior syphilis laboratory test results was not provided by the vendor.

One of the 10 CMV IgG specimens, 1 of the 10 HIV specimens, 1 of the 7 monoclonal hyper IgG, and 1 of the 10 anti-*E. coli* specimens (marked by <sup>b</sup> in table below) were reactive in ARCHITECT Syphilis TP and were not confirmed with other treponemal or nontreponemal tests applied in this study.

One of the 11 gonorrhea specimens and 2 of the 6 HTLV-II specimens (marked by <sup>c</sup> in table below) were reactive in ARCHITECT Syphilis TP but could not be tested by the other tests (TP-CLIA, RPR, TP-PA, Fluorescent Treponemal Antibody Absorption [FTA-ABS]) because specimens from these disease states could only be sourced as plasma specimens.

<b>Clinical Category</b>	<b>N</b>	<b>Number of ARCHITECT Syphilis TP Reactive Results</b>
Chlamydia	15	1 <sup>a</sup>
Cytomegalovirus (CMV) IgG	10	1 <sup>b</sup>
Cytomegalovirus (CMV) IgM	10	1 <sup>a</sup>
Anti-dsDNA Autoantibodies	3	0
Epstein-Barr Virus (EBV) IgG	10	1 <sup>a</sup>
Epstein-Barr Virus (EBV) IgM	24	0
Anti- <i>Escherichia coli</i> ( <i>E. coli</i> )	10	1 <sup>b</sup>

<b>Clinical Category</b>	<b>N</b>	<b>Number of ARCHITECT Syphilis TP Reactive Results</b>
Gonorrhea	11	1 <sup>c</sup>
HAVAB IgG	10	0
HBc IgM	4	0
Hemodialysis	10	0
Hepatitis A Virus (HAV)	10	1 <sup>a</sup>
Hepatitis B Virus (HBV)	10	0
Hepatitis C Virus (HCV)	10	1 <sup>a</sup>
Herpes Simplex Virus (HSV)	10	1 <sup>d</sup>
Human Anti-Mouse Antibodies (HAMA)	10	0
Human Immunodeficiency Virus (HIV)	10	1 <sup>b</sup>
Human T-Lymphotropic Virus-I (HTLV-I)	10	0
Human T-Lymphotropic Virus-II (HTLV-II)	6	2 <sup>c</sup>
Influenza Vaccine Recipient	20	0
Leptospirosis	6	0
Leptospirosis IgM	5	0
Lyme Disease	10	0
Monoclonal Hyper IgG	7	1 <sup>b</sup>
Anti-Nuclear Antibody (ANA)	10	0
Polyclonal Hyper IgG	3	0
Pregnant	90	0
Rheumatoid Factor	10	0
Rubella IgG	10	0
Systemic Lupus Erythematosus	10	0
<i>Toxoplasma gondii</i> IgG	12	0
<i>Toxoplasma gondii</i> IgM	3	0
Transplant Recipient	10	0
Varicella Zoster Virus	10	0
<b>Total</b>	<b>409</b>	<b>13</b>

<sup>a</sup> Specimen was confirmed to be positive by other tests (TP-CLIA, RPR, TP-PA, FTA-ABS).

<sup>b</sup> Specimen was not confirmed positive by other tests (TP-CLIA, RPR, TP-PA, FTA-ABS).

<sup>c</sup> Specimen was reactive by ARCHITECT Syphilis TP but was not confirmed due to tube type limitations of the other tests (TP-CLIA, RPR, TP-PA, FTA-ABS).

<sup>d</sup> Specimen was positive by TP-CLIA and indeterminate by TP-PA and FTA-ABS.

Assay interference due to circulating antibodies against yaws, pinta, and bejel has not been evaluated. Cross-reactivity with these conditions is to be expected. Therefore, the following statement will be included in the Limitations section of the ARCHITECT Syphilis TP reagent package insert: “Assay interference due to circulating antibodies against yaws, pinta, and bejel has not been evaluated. Cross-reactivity with these treponemal disease conditions is to be expected.”

## Tube Type Matrix Comparison

The following tube types are acceptable for use with the ARCHITECT Syphilis TP assay:

- Serum, including serum separator
- Plasma: dipotassium EDTA, tripotassium EDTA, lithium heparin plasma separator, lithium heparin, and sodium heparin

The ARCHITECT Syphilis TP assay showed the following mean/median S/CO difference and distribution of S/CO difference for nonreactive samples when compared to the control tube type (serum).

Tube Type	Nonreactive Samples (Unspiked)					High Nonreactive Samples (Target 0.80 S/CO)				
	N	Mean/ Median S/CO Difference <sup>a</sup>	Distribution of S/CO Differences			N	Mean/ Median S/CO Difference <sup>a</sup>	Distribution of S/CO Differences		
			< 0.10 S/CO	0.10–0.20 S/CO	> 0.20 S/CO			< 0.10 S/CO	0.10–0.20 S/CO	> 0.20 S/CO
Serum Separator, Plastic	28	0.00	100.0% (28/28)	0.0% (0/28)	0.0% (0/28)	27	0.02	81.5% (22/27)	18.5% (5/27)	0.0% (0/27)
Dipotassium EDTA	28	-0.00	100.0% (28/28)	0.0% (0/28)	0.0% (0/28)	27	0.02	81.5% (22/27)	18.5% (5/27)	0.0% (0/27)
Tripotassium EDTA	27	-0.00	100.0% (27/27)	0.0% (0/27)	0.0% (0/27)	27	0.02	85.2% (23/27)	11.1% (3/27)	3.7% (1/27)
Lithium Heparin Plasma Separator	28	-0.01	100.0% (28/28)	0.0% (0/28)	0.0% (0/28)	27	0.01	88.9% (24/27)	11.1% (3/27)	0.0% (0/27)
Lithium Heparin	28	-0.01	100.0% (28/28)	0.0% (0/28)	0.0% (0/28)	27	0.02	88.9% (24/27)	7.4% (2/27)	3.7% (1/27)
Sodium Heparin	28	-0.01	100.0% (28/28)	0.0% (0/28)	0.0% (0/28)	26	0.00	88.5% (23/26)	11.5% (3/26)	0.0% (0/26)

<sup>a</sup> If the Shapiro-Wilk p-value is  $\leq 0.0100$ , then the value displayed is the median.

The ARCHITECT Syphilis TP assay showed the following mean/median percent difference and distribution of percent difference for reactive samples when compared to the control tube type (serum).

Tube Type	Low Reactive Samples (Target 1.20 S/CO)					High Reactive Samples (Target 6.00 S/CO)				
	N	Mean/Median % Difference <sup>a</sup>	Distribution of % Differences			N	Mean/Median % Difference <sup>a</sup>	Distribution of % Differences		
			< 10%	10–20%	> 20%			< 10%	10–20%	> 20%
Serum Separator, Plastic	28	0.3	96.4% (27/28)	3.6% (1/28)	0.0% (0/28)	28	-0.1	96.4% (27/28)	3.6% (1/28)	0.0% (0/28)
Dipotassium EDTA	28	0.9	100.0% (28/28)	0.0% (0/28)	0.0% (0/28)	28	-0.7	100.0% (28/28)	0.0% (0/28)	0.0% (0/28)
Tripotassium EDTA	28	-0.0	96.4% (27/28)	3.6% (1/28)	0.0% (0/28)	27	-0.3	100.0% (27/27)	0.0% (0/27)	0.0% (0/27)
Lithium Heparin Plasma Separator	27	3.7	63.0% (17/27)	33.3% (9/27)	3.7% (1/27)	28	-0.1	100.0% (28/28)	0.0% (0/28)	0.0% (0/28)
Lithium Heparin	28	-0.3	96.4% (27/28)	3.6% (1/28)	0.0% (0/28)	28	-0.0	100.0% (28/28)	0.0% (0/28)	0.0% (0/28)
Sodium Heparin	28	0.8	96.4% (27/28)	3.6% (1/28)	0.0% (0/28)	28	-0.3	100.0% (28/28)	0.0% (0/28)	0.0% (0/28)

<sup>a</sup> If the Shapiro-Wilk p-value is  $\leq 0.0100$ , then the value displayed is the median.

### Sample On-Board Stability

A study was performed to evaluate the stability of samples when stored on the ARCHITECT i2000SR System (on-board storage) and tested with the ARCHITECT Syphilis TP assay.

Samples may be stored on-board the ARCHITECT instrument for up to 3 hours.

### Sample Stability

A study was performed to evaluate serum and plasma specimens when subjected to various conditions (room temperature storage, 2 to 8°C storage, and freeze/thaw) and tested with the ARCHITECT Syphilis TP assay.

Specimens may be stored before testing

- for up to 7 days after draw at 2 to 8°C (on the cells/clot)
- for up to 72 hours after draw at room temperature (30°C) (on the cells/clot)

After storage at 2 to 8°C off the cells/clot, specimens can be subjected to up to 6 freeze/thaw cycles.

After storage at 2 to 8°C off the cells/clot, specimens can be stored frozen (-10°C or colder) for up to 30 days before testing.

### **High Dose Hook Effect**

A study was performed that demonstrated that the ARCHITECT Syphilis TP assay is not susceptible to interference from specimens with high levels of anti-syphilis TP.

### **Within-Assay Sample Carryover**

A study was performed to evaluate the susceptibility of the ARCHITECT Syphilis TP assay to within-assay sample carryover from a sample containing a very high level of syphilis anti-TP antibodies.

The ARCHITECT Syphilis TP assay is not susceptible to within-assay sample carryover.

## VIII. Summary of Clinical Performance

### EXPECTED VALUES

Due to geographic locations or demographics, assay results obtained in individual laboratories may vary from data presented.

A total of 1145 specimens prospectively collected from the intended use population were tested using the ARCHITECT Syphilis TP assay; 673 (58.8%) were female and 472 (41.2%) were male. The mean age was 35 years (age range: 6 to 91 years).

The ARCHITECT Syphilis TP assay was reactive in 163 (14.2 %) of the prospectively-collected specimens in the intended use population. Testing of the specimens was performed at three clinical testing sites located in San Antonio, Texas; Baltimore, Maryland; and Temple, Texas.

The distribution of ARCHITECT Syphilis TP reactive and nonreactive results by age and gender is summarized in the following table.

Age Range (Years)	Gender	ARCHITECT Syphilis TP Result		Total
		Number of Reactive (%)	Number of Nonreactive (%)	
2 to 12	Female	0 (0.0%)	1 (100.0%)	1
13 to 21	Female	1 (0.8%)	118 (99.2%)	119
	Male	1 (6.3%)	15 (93.8%)	16
22 to 29	Female	6 (2.6%)	229 (97.4%)	235
	Male	12 (23.5%)	39 (76.5%)	51
30 to 39	Female	6 (2.9%)	199 (97.1%)	205
	Male	32 (23.7%)	103 (76.3%)	135
40 to 49	Female	9 (12.9%)	61 (87.1%)	70
	Male	50 (29.6%)	119 (70.4%)	169
50 to 59	Female	5 (21.7%)	18 (78.3%)	23
	Male	29 (40.8%)	42 (59.2%)	71
60 to 64	Female	3 (50.0%)	3 (50.0%)	6
	Male	2 (16.7%)	10 (83.3%)	12

Age Range (Years)	Gender	ARCHITECT Syphilis TP Result		Total
		Number of Reactive (%)	Number of Nonreactive (%)	
65 to 100	Female	1 (7.1%)	13 (92.9%)	14
	Male	6 (33.3%)	12 (66.7%)	18
<b>Total</b>		163 (14.2%)	982 (85.8%)	1145

The 1145 prospectively-collected specimens from the intended use population included 442 specimens sent for routine syphilis testing (325 female and 117 male, 6–91 years old), 304 pregnant females (16–43 years old), and 399 human immunodeficiency virus (HIV) positive individuals (44 female and 355 male, 18–72 years old).

The ARCHITECT Syphilis TP results for each category in the intended use population are summarized in the following table.

Category	ARCHITECT Syphilis TP Result		
	Number of Reactive (%)	Number of Nonreactive (%)	Total
Routine Syphilis	38 (8.6%)	404 (91.4%)	442
Pregnant	1 (0.3%)	303 (99.7%)	304
HIV Positive	124 (31.1%)	275 (68.9%)	399
<b>Total</b>	163 (14.2%)	982 (85.8%)	1145

## Precision

### System Reproducibility

A 5-day precision study was performed for the ARCHITECT Syphilis TP assay based on guidance from CLSI documents EP05-A2 and EP15-A2. Testing was conducted at 3 clinical sites using 3 lots each of ARCHITECT Syphilis TP Reagents, 2 lots of ARCHITECT Syphilis TP Calibrator, and 1 lot of ARCHITECT Syphilis TP Controls, on 1 instrument per site. Two levels of controls and 4 serum panels were assayed in replicates of 4 at 2 separate times of day for 5 days.

Sample	N	Grand Mean S/CO	Within-Run		Within-Day		Within-Laboratory (Total)			Precision with Additional Component of Between-Site		Precision with Additional Component of Between-Lot		Precision with Additional Components of Site and Lot (Overall)	
			SD	%CV	SD	%CV	SD	%CV	95% CI	SD	%CV	SD	%CV	SD	%CV
Negative Control	360	0.03	0.002	6.4	0.002	6.6	0.002	6.6	(6.24,7.08)	0.003	9.3	0.003	9.5	0.003	9.6
Positive Control <sup>a</sup>	360	2.72	0.108	4.0	0.130	4.8	0.134	4.9	(4.59,5.35)	0.134	4.9	0.134	4.9	0.134	4.9
Nonreactive Panel	360	0.08	0.004	5.1	0.004	5.1	0.004	5.4	(5.07,5.78)	0.006	7.5	0.006	7.4	0.007	8.8
High Nonreactive Panel	360	0.55	0.012	2.3	0.015	2.7	0.015	2.8	(2.61,3.04)	0.017	3.2	0.017	3.2	0.017	3.2
Low Reactive Panel	360	1.24	0.023	1.9	0.027	2.2	0.029	2.4	(2.18,2.56)	0.034	2.7	0.035	2.8	0.035	2.8
High Reactive Panel	360	3.57	0.073	2.0	0.079	2.2	0.094	2.6	(2.43,2.91)	0.107	3.0	0.100	2.8	0.107	3.0

<sup>a</sup> An outlying run was observed at one site for one reagent lot. The total %CV for the Positive Control using the replacement run was 2.6%.

## Clinical Performance

A multicenter study was conducted on the ARCHITECT iSystem to evaluate the ability of the ARCHITECT Syphilis TP assay to detect antibodies (IgG and IgM) directed against *Treponema pallidum* (TP).

A total of 2222 specimens were tested in the ARCHITECT Syphilis TP clinical study. Two specimens were excluded due to specimen issues. The remaining 2220 specimens included 1145 prospectively collected from the intended use population; 406 pre-selected positive for antibodies directed against TP based on previous laboratory testing (including 20 pregnant women known to be reactive for syphilis antibodies); 480 from apparently healthy individuals; 179 from medically diagnosed individuals with primary, secondary, or latent syphilis; and 10 specimens from pregnant females spiked with high antibody-positive syphilis TP specimens.

Each specimen prospectively collected from the intended use population or pre-selected positive for antibodies directed against TP based on previous laboratory testing was tested using the ARCHITECT Syphilis TP assay and the following comparator assays: a treponemal chemiluminescent immunoassay (TP-CLIA), a nontreponemal assay (Rapid Plasma Reagin [RPR]), and a second treponemal assay (Treponema Pallidum Particle Agglutination [TP-PA]). The final comparator result was determined using a 2 out of 3 rule (TP-CLIA, RPR, and TP-PA).

The clinical performance of the ARCHITECT Syphilis TP assay was evaluated by calculating positive percent agreement and negative percent agreement of the assay with the final comparator result.

During the clinical study (total number of tests = 2220), 2 exception codes prevented initial results and were retested to generate a final result.

**Clinical Performance in Prospectively-Collected Specimens in Intended Use Population**

Of the total 2220 specimens analyzed in the ARCHITECT Syphilis TP clinical study, 1145 were prospectively-collected intended use population specimens. These included 442 specimens sent for routine syphilis testing (325 female and 117 male, 6–91 years old), 304 pregnant females (16–43 years old), and 399 HIV positive (44 female and 355 male, 18–72 years old). Of the 1145 prospectively-collected specimens in the intended use population, 136 were pediatric specimens (6–21 years old).

The 1145 specimens included in the intended use population were prospectively sourced or collected at the following locations:

- Baltimore, Maryland: 12.4%
- Colton, California: 5.9%
- Fort Lauderdale, Florida: 7.8%
- Hyannis, Massachusetts: 0.1%
- Los Angeles, California: 19.7%
- Miami, Florida: 27.2%
- San Antonio, Texas: 11.5%
- Temple, Texas: 14.8%
- Location Unknown: 0.4%

A summary of the serological test profile for all prospectively-collected specimens in the intended use population is summarized in the following table.

<b>TP-CLIA</b>	<b>RPR</b>	<b>TP-PA</b>	<b>Final Comparator Result</b>	<b>ARCHITECT</b>	<b>Number of Subjects</b>
+	+	+	+	+	113
+	+	I	+	+	1

TP-CLIA	RPR	TP-PA	Final Comparator Result	ARCHITECT	Number of Subjects
+	-	+	+	+	37
+	-	-	-	-	4
+	-	-	-	+	2
-	+	+	+	-	6
-	+	+	+	+	1
-	+	-	-	-	167
-	+	-	-	+	3
-	+	I	-	-	1 <sup>a</sup>
-	+	I	-	+	1 <sup>a</sup>
-	-	+	-	-	8
-	-	+	-	+	2
-	-	-	-	-	796
-	-	-	-	+	2
E	-	+	+	+	1 <sup>b</sup>
<b>Total</b>					1145

+ = Positive/Reactive

- = Negative/Nonreactive

E = Equivocal

I = Inconclusive

<sup>a</sup> Two specimens that were TP-CLIA nonreactive, RPR reactive, and TP-PA inconclusive were assigned a final comparator result of negative based on the nonreactive treponemal test.

<sup>b</sup> One specimen that was TP-CLIA equivocal, RPR nonreactive, and TP-PA reactive was assigned a final comparator result of positive based on the reactive treponemal test.

### Percent Agreement

The comparison between the ARCHITECT Syphilis TP result and the final comparator result for the prospectively-collected specimens in the intended use population is summarized in the following table.

ARCHITECT Syphilis TP Result Interpretation	Final Comparator Result	
	Reactive	Nonreactive
Reactive	153	10
Nonreactive	6 <sup>a</sup>	976

<sup>a</sup> Six specimens were nonreactive by TP-CLIA and reactive by TP-PA and RPR.

Positive percent agreement was 96.2% (153/159) with a 95% confidence interval of 92.0% to 98.3%. Negative percent agreement was 99.0% (976/986) with a 95% confidence interval of 98.1% to 99.4%.

Percent Agreement by Category

The percent agreement between the ARCHITECT Syphilis TP result and the final comparator result for each category of the prospectively-collected specimens in the intended use population is summarized in the following table.

<b>Category</b>	<b>Positive Percent Agreement % (x/n)</b>	<b>95% Confidence Interval (%)</b>	<b>Negative Percent Agreement % (x/n)</b>	<b>95% Confidence Interval (%)</b>
Routine Syphilis	97.3 (36/37)	86.2–99.5	99.5 (403/405)	98.2–99.9
Pregnant	NA	NA	99.7 (303/304)	98.2–99.9
HIV Positive	95.9 (117/122)	90.8–98.2	97.5 (270/277)	94.9–98.8

NA = not applicable

**Clinical Performance in Pre-Selected Positive Specimens**

Of the total 2220 specimens analyzed in the ARCHITECT Syphilis TP clinical study, 406 specimens were pre-selected positive for antibodies directed against TP based on previous laboratory testing (RPR and/or TP-PA). These included 386 presumed positive (106 female and 278 male, 16–78 years old). Gender was not reported for 2 specimens. Pre-selected positive specimens also included 20 reactive pregnant female specimens (17–36 years old). Of the 406 pre-selected positive specimens, 25 were pediatric specimens (16–21 years old).

A summary of the serological test profile for all pre-selected positive specimens is summarized in the following table.

<b>TP-CLIA</b>	<b>RPR</b>	<b>TP-PA</b>	<b>Final Comparator Result</b>	<b>ARCHITECT</b>	<b>Number of Subjects</b>
+	+	+	+	+	259
+	+	I	+	+	1
+	-	+	+	-	2

TP-CLIA	RPR	TP-PA	Final Comparator Result	ARCHITECT	Number of Subjects
+	-	+	+	+	116
+	-	-	-	-	1
+	-	-	-	+	2
+	-	I	+	-	1 <sup>a</sup>
-	+	-	-	-	3
-	-	-	-	-	20
E	-	+	+	-	1 <sup>b</sup>
<b>Total</b>					406

+ = Positive/Reactive

- = Negative/Nonreactive

E = Equivocal

I = Inconclusive

a One specimen that was TP-CLIA reactive, RPR nonreactive, and TP-PA inconclusive was assigned a final comparator result of positive based on the reactive treponemal test.

b One specimen that was TP-CLIA equivocal, RPR nonreactive, and TP-PA reactive was assigned a final comparator result of positive based on the reactive treponemal test.

#### Percent Agreement

The comparison between the ARCHITECT Syphilis TP result and the final comparator result for all pre-selected positive specimens is summarized in the following table.

ARCHITECT Syphilis TP Result Interpretation	Final Comparator Result	
	Reactive	Nonreactive
Reactive	376	2
Nonreactive	4	24

Positive percent agreement was 98.9% (376/380) with a 95% confidence interval of 97.3% to 99.6%. Negative percent agreement was 92.3% (24/26) with a 95% confidence interval of 75.9% to 97.9%.

### Percent Agreement by Category

The percent agreement between the ARCHITECT Syphilis TP result and the final comparator result for each category in the pre-selected positive population is summarized in the following table.

<b>Category</b>	<b>Positive Percent Agreement % (x/n)</b>	<b>95% Confidence Interval (%)</b>	<b>Negative Percent Agreement % (x/n)</b>	<b>95% Confidence Interval (%)</b>
Presumed Positive	98.9 (356/360)	97.2–99.6	92.3 (24/26)	75.9–97.9
Reactive Pregnant	100.0 (20/20)	83.9–100.0	NA	NA

NA = not applicable

### Clinical Performance in Apparently Healthy Individuals

Of the total 2220 specimens analyzed in the ARCHITECT Syphilis TP clinical study, 480 specimens were from apparently healthy individuals. These included 244 female and 236 male, adults (22–89 years old), and pediatrics (0–21 years old).

<b>Category</b>	<b>ARCHITECT Syphilis TP Result</b>		
	<b>Number of Reactive (%)</b>	<b>Number of Nonreactive (%)</b>	<b>Total</b>
Adults	15 (4.1%) <sup>a</sup>	352 (95.9%)	367
Pediatrics	0 (0.0%)	113 (100.0%)	113
<b>Total</b>	15 (3.1%)	465 (96.9%)	480

<sup>a</sup> Fourteen specimens were reactive and 1 specimen was equivocal by TP-CLIA.

### **Clinical Performance in Medically Diagnosed Individuals**

Of the total 2220 specimens analyzed in the ARCHITECT Syphilis TP clinical study, 179 were from individuals medically diagnosed with primary, secondary, or latent syphilis. Medical diagnosis was made by a licensed physician based on the patient's clinical information and the results of serological testing, such as a positive test for syphilis (Venereal Disease Research Laboratory [VDRL] test, RPR, and/or TP-PA) at the time the specimen was collected. These included 9 female and 170 male, adults (22–66 years old), and pediatrics (18–21 years old).

<b>Medically Diagnosed Individuals</b>			<b>ARCHITECT Syphilis TP Result</b>	
<b>Syphilis Stage</b>	<b>Treatment Status</b>	<b>N</b>	<b>Reactive</b>	<b>Nonreactive</b>
Primary	Treated	44	33	11 <sup>a</sup>
	Untreated	25	25	0
Secondary	Treated	29	29	0
	Untreated	27	27	0
Latent	Treated	25	25	0
	Untreated	29	29	0

<sup>a</sup> Nine specimens were nonreactive by TP-CLIA.

## **CLINICAL PERFORMANCE IN PREGNANT FEMALES**

A total of 334 pregnant female specimens were analyzed in the ARCHITECT Syphilis TP clinical study. These included adults (22–43 years old) and pediatrics (16–21 years old). Age was not reported for 10 specimens.

The percent agreement for the prospectively-collected and the pre-selected positive specimens between the ARCHITECT Syphilis TP results and the final comparator results for the pregnant female population by trimester is summarized in the following table.

<b>Category</b>	<b>Positive Percent Agreement % (x/n)</b>	<b>95% Confidence Interval (%)</b>	<b>Negative Percent Agreement % (x/n)</b>	<b>95% Confidence Interval (%)</b>
Prospectively-Collected	NA	NA	99.7 (303/304)	98.2–99.9
First Trimester	NA	NA	100.0 (13/13)	77.2–100.0
Second Trimester <sup>a</sup>	NA	NA	99.2 (126/127)	95.7–99.9
Third Trimester	NA	NA	100.0 (161/161)	97.7–100.0
Trimester Unknown	NA	NA	100.0 (3/3)	43.8–100.0
Pre-Selected Positive	100.0 (20/20)	83.9–100.0	NA	NA
First Trimester	100.0 (1/1)	20.7–100.0	NA	NA
Second Trimester	NA	NA	NA	NA
Third Trimester	100.0 (5/5)	56.6–100.0	NA	NA
Trimester Unknown	100.0 (14/14)	78.5–100.0	NA	NA

NA = not applicable

<sup>a</sup> One specimen reactive on ARCHITECT was reactive by TP-CLIA and nonreactive by RPR and TP-PA.

In addition, 10 nonreactive pregnant female specimens that were spiked with high antibody-positive syphilis TP specimens were reactive by ARCHITECT Syphilis TP and TP-CLIA. Positive percent agreement was 100.0% with a confidence interval of 72.2% to 100.0%.

Conclusion Drawn from Nonclinical and Clinical Laboratory Studies

The results presented in this 510(k) premarket notification demonstrate that the candidate assay (ARCHITECT Syphilis TP [List No. 8D06]) performance is substantially equivalent to the predicate assay (DiaSorin LIAISON Treponema assay, k061247).

The similarities and differences between the candidate assay and the predicate assay are presented in the tables starting on [page 5-5](#).

There is no known potential adverse effect to the operator when using this *in vitro* device according to the ARCHITECT Syphilis TP reagent package insert instructions.