ARCHITECT SYSTEM

en

Syphilis TP

REF 8D06

F5-Y203-2/R1

Syphilis TP

Customer Service: Contact your local representative or find country specific contact information on www.abbottdiagnostics.com

Package insert instructions must be carefully followed. Reliability of assay results cannot be guaranteed if there are any deviations from the instructions in this package insert.

Key to symbols used

REF	List Number	REAGENT LOT	Reagent Lot
IVD	*In Vitro* Diagnostic Medical Device	SN	Serial Number
LOT	Lot Number	REACTION VESSELS	Reaction Vessels
	Expiration Date	SAMPLE CUPS	Sample Cups
2°C 8°C	Store at 2-8°C	SEPTUM	Septum
		REPLACEMENT CAPS	Replacement Caps
	Consult instructions for use	ASSAY CD-ROM	Assay CD-ROM
	Manufacturer	CONTROL NO.	Control Number

See **REAGENTS** section for a full explanation of symbols used in reagent component naming.

Abbott

NAME

ARCHITECT Syphilis TP

INTENDED USE

The ARCHITECT Syphilis TP assay is a chemiluminescent microparticle immunoassay (CMIA) for the qualitative detection of antibody to *Treponema pallidum* (TP) in human serum and plasma on the ARCHITECT *i* System as an aid to diagnosis of syphilis.

SUMMARY AND EXPLANATION OF TEST

Syphilis is caused by infection with the bacterium TP[1] which can be transmitted congenitally or by sexual contact. The disease can evolve into a latent phase in which syphilis is clinically inapparent. Serological tests (nontreponemal and treponemal specific), in addition to patients' clinical history, are currently the primary methods for the diagnosis and management of syphilis.

BIOLOGICAL PRINCIPLES OF THE PROCEDURE

The ARCHITECT Syphilis TP assay is a two-step immunoassay for the qualitative detection of antibody to TP in human serum or plasma using CMIA technology with flexible assay protocols, referred to as Chemiflex. In the first step, sample, microparticles coated with recombinant TP antigens (TpN15, TpN17 and TpN47) and Assay Diluent are combined. Anti-TP antibodies present in the sample bind to the TP coated microparticles. After washing, the acridinium-labeled anti-human IgG and IgM conjugate is added in the second step. Following another wash cycle, Pre-Trigger and Trigger Solutions are added to the reaction mixture. The resulting chemiluminescent reaction is measured as relative light units (RLUs). A direct relationship exists between the amount of anti-TP antibodies in the sample and the RLUs detected by the ARCHITECT *i** optical system.

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 a previous ARCHITECT Syphilis TP calibration. If the chemiluminescent signal in the specimen is greater than or equal to the cutoff signal, the specimen is considered reactive for anti-TP.

For additional information on system and assay technology, refer to the ARCHITECT System Operations Manual, Section 3.

* *i* = immunoassay

REAGENTS

Reagent Kit, 100 Tests/500 Tests

NOTE: Some kit sizes are not available in all countries or for use on all ARCHITECT *i* Systems. Please contact your local distributor.

ARCHITECT Syphilis TP Reagent Kit (8D06)

- **MICROPARTICLES** 1 Bottle (6.6 mL per 100 test bottle/27.0 mL per 500 test bottle) Microparticles: TP (*E.coli,* recombinant) antigen coated microparticles in MES buffer. Minimum concentration: 0.08% solids. Preservatives: sodium azide and other antimicrobial agents.
- **CONJUGATE** 1 Bottle (5.9 mL per 100 test bottle/26.3 mL per 500 test bottle) Conjugate: 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 (10.0 mL per 100 test bottle/52.5 mL per 500 test bottle) Syphilis TP Assay Diluent containing MES buffer. Preservatives: sodium azide and other antimicrobial agent.

Other Reagents

ARCHITECT *i* Pre-Trigger Solution

- **PRE-TRIGGER SOLUTION** Pre-Trigger Solution containing 1.32% (w/v) hydrogen peroxide.

ARCHITECT *i* Trigger Solution

- **TRIGGER SOLUTION** Trigger Solution containing 0.35 N sodium hydroxide.

ARCHITECT *i* Wash Buffer

- **WASH BUFFER** Wash Buffer containing phosphate buffered saline solution. Preservatives: antimicrobial agents.

WARNINGS AND PRECAUTIONS

- **IVD**
- For *In Vitro* Diagnostic Use
- Package insert instructions must be carefully followed. Reliability of assay results cannot be guaranteed if there are any deviations from the instructions in this package insert.

Safety Precautions

- **CAUTION:** This product requires the handling of human specimens. It is recommended that all human sourced materials be considered potentially infectious and handled in accordance with the OSHA Standard on Bloodborne Pathogens.[2] Biosafety Level 2[3] or other appropriate biosafety practices[4,5] should be used for materials that contain or are suspected of containing infectious agents.
- This product contains sodium azide; for a specific listing, refer to the **REAGENTS** section. Contact with acids liberates very toxic gas. This material and its container must be disposed of in a safe way.
- For product not classified as dangerous per European Directive 1999/45/EC as amended - Safety data sheet available for professional user on request.
- For information on the safe disposal of sodium azide and a detailed discussion of safety precautions during system operation, refer to the ARCHITECT System Operations Manual, Section 8.

Handling Precautions

- Do not use reagent kits beyond the expiration date.
- **Do not pool reagents within a kit or between reagent kits.**
- Before loading the ARCHITECT Syphilis TP Reagent Kit on the system for the first time, the microparticle bottle requires mixing to resuspend microparticles that have settled during shipment. For microparticle mixing instructions, refer to the **PROCEDURE, Assay Procedure** section of this package insert.
- **Septums MUST be used to prevent reagent evaporation and contamination and to ensure reagent integrity. Reliability of assay results cannot be guaranteed if septums are not used according to the instructions in this package insert.**
- To avoid contamination, wear clean gloves when placing a septum on an uncapped reagent bottle.
  - When handling conjugate vials, change gloves that have contacted human serum or plasma, since introduction of human IgG/IgM will result in a neutralized conjugate.
  - Once a septum has been placed on an open reagent bottle, **do not invert the bottle** as this will result in reagent leakage and may compromise assay results.
  - Over time, residual liquids may dry on the septum surface. These are typically dried salts which have no effect on assay efficacy.
- For a detailed discussion of handling precautions during system operation, refer to the ARCHITECT System Operations Manual, Section 7.

Storage Instructions

- The ARCHITECT Syphilis TP Reagent Kit must be stored at 2-8˚C in an upright position and may be used immediately after removal from 2-8˚C storage.
- When stored and handled as directed, reagents are stable until the expiration date.
- The ARCHITECT Syphilis TP Reagent Kit may be stored on board the ARCHITECT *i* System for a maximum of 30 days. After 30 days, the reagent kit must be discarded. For information on tracking onboard time, refer to the ARCHITECT System Operations Manual, Section 5.
- Reagents may be stored on or off the ARCHITECT *i* System. If reagents are removed from the system, store them at 2-8˚C (with septums and replacement caps) in an upright position. For reagents stored off the system, it is recommended that they be stored in their original trays and boxes to ensure they remain upright. **If the microparticle bottle does not remain upright (with a septum installed) while in refrigerated storage off the system, the reagent kit must be discarded.** For information on unloading reagents, refer to the ARCHITECT System Operations Manual, Section 5.

Indications of Reagent Deterioration

When a control value is out of the specified range, it may indicate deterioration of the reagents or errors in technique. Associated test results are invalid and samples must be retested. Assay recalibration may be necessary. For troubleshooting information, refer to the ARCHITECT System Operations Manual, Section 10.

INSTRUMENT PROCEDURE

- The ARCHITECT Syphilis TP assay file must be installed on the ARCHITECT *i* System from the ARCHITECT *i* Assay CD-ROM (Addition C) prior to performing the assay. For detailed information on assay file installation and on viewing and editing assay parameters, refer to the ARCHITECT System Operations Manual, Section 2.
- For information on printing assay parameters, refer to the ARCHITECT System Operations Manual, Section 5.
- For a detailed description of system procedures, refer to the ARCHITECT System Operations Manual.

SPECIMEN COLLECTION AND PREPARATION FOR ANALYSIS

Specimen Types

The specimen collection tubes listed below were verified to be used with the ARCHITECT Syphilis TP assay. Other specimen collection tubes have not been tested with this assay.

- Human serum (including serum collected in serum separator tubes)
- Human plasma collected in:
  - Potassium EDTA
  - Lithium heparin
  - Sodium heparin
  - Sodium citrate
  - CPD
- Liquid anticoagulants may have a dilution effect resulting in lower concentrations for individual patient specimens.
- The ARCHITECT *i* System does not provide the capability to verify specimen type. It is the responsibility of the operator to verify that the correct specimen types are used in the ARCHITECT Syphilis TP assay.

Specimen Conditions

- Do not use specimens with the following conditions:
  - heat-inactivated
  - grossly hemolyzed (> 500 mg/dL)
  - obvious microbial contamination
  - cadaver specimens or any other body fluids
- For accurate results, serum and plasma specimens should be free of fibrin, red blood cells, and other particulate matter. Serum specimens from patients receiving anticoagulant or thrombolytic therapy may contain fibrin due to incomplete clot formation.
- Use caution when handling patient specimens to prevent cross contamination. Use of disposable pipettes or pipette tips is recommended.
- For optimal results, inspect all specimens for bubbles. Remove bubbles with an applicator stick before analysis. Use a new applicator stick for each specimen to prevent cross contamination.

Preparation for Analysis

- Follow the tube manufacturer's processing instructions for serum and plasma collection tubes. Gravity separation is not sufficient for specimen preparation.
- Mix thawed specimens thoroughly by low speed vortexing or by inverting 10 times. Visually inspect the specimens. If layering or stratification is observed, continue mixing until specimens are visibly homogeneous.
- To ensure consistency in results, specimens must be transferred to a centrifuge tube and centrifuged at ≥ 10000 RCF (Relative Centrifugal Force) for 10 minutes before testing if
  - they contain fibrin, red blood cells, or other particulate matter,
  - they require repeat testing, or
  - they were frozen and thawed.

  Transfer clarified specimen to a sample cup or secondary tube for testing.
- Centrifuged specimens with a lipid layer on the top must be transferred to a sample cup or secondary tube. Care must be taken to transfer only the clarified specimen without the lipemic material.

Storage

- If testing will be delayed, serum or plasma should be removed from the clot, red blood cells, or separator gel. Specimens may be stored for 24 hours at room temperature or up to 7 days at 2-8°C.
- Avoid multiple freeze/thaw cycles.

Shipping

- Before shipping specimens, it is recommended that specimens be removed from the clot, red blood cells, or separator gel.
- When shipping specimens, package and label specimens in compliance with applicable state, federal, and international regulations covering the transport of clinical specimens and infectious substances.
- Specimens may be shipped on wet or dry ice. Do not exceed the storage time limitations listed above.

PROCEDURE

Materials Provided

- 8D06 ARCHITECT Syphilis TP Reagent Kit

Materials Required but not Provided

- ARCHITECT *i* System
- ARCHITECT *i* **ASSAY CD-ROM** Addition C Version 3.0 or higher
- 8D06-02 ARCHITECT Syphilis TP Calibrator
- 8D06-11 ARCHITECT Syphilis TP Controls
- ARCHITECT *i* **PRE-TRIGGER SOLUTION**
- ARCHITECT *i* **TRIGGER SOLUTION**
- ARCHITECT *i* **WASH BUFFER**
- ARCHITECT *i* **REACTION VESSELS**
- ARCHITECT *i* **SAMPLE CUPS**
- ARCHITECT *i* **SEPTUM**
- ARCHITECT *i* **REPLACEMENT CAPS**
- Pipettes or pipette tips (optional)

For information on materials required for maintenance procedures, refer to the ARCHITECT System Operations Manual, Section 9.

Assay Procedure

- Before loading the ARCHITECT Syphilis TP Reagent Kit on the system for the first time, the microparticle bottle requires mixing to resuspend microparticles that have settled during shipment. After the first time the microparticles have been loaded, no further mixing is required.
  - **Invert the microparticle bottle 30 times.**
  - Visually inspect the bottle to ensure microparticles are resuspended. If microparticles remain adhered to the bottle, continue inverting the bottle until the microparticles have been completely resuspended.
  - **If the microparticles do not resuspend, DO NOT USE. Contact your local Abbott representative.**
  - Once the microparticles have been resuspended, place a septum on the bottle. For instructions on placing septums on bottles refer to the **Handling Precautions** section of this package insert.
- Load the ARCHITECT Syphilis TP Reagent Kit on the ARCHITECT *i* System.
  - Verify that all necessary assay reagents are present.
  - Ensure that septums are present on all reagent bottles.
- Order calibration, if necessary.
  - For information on ordering calibrations, refer to the ARCHITECT System Operations Manual, Section 6.
- Order tests.
  - For information on ordering patient specimens and controls and for general operating procedures, refer to the ARCHITECT System Operations Manual, Section 5.
- The minimum sample cup volume is calculated by the system and is printed on the Orderlist report. No more than 10 replicates may be sampled from the same sample cup. To minimize the effects of evaporation, verify adequate sample cup volume is present before running the test.

- Priority: 150 µL for the first ARCHITECT Syphilis TP test plus 30 µL for each additional ARCHITECT Syphilis TP test from the same sample cup.
- ≤ 3 hours on board: 150 µL for the first ARCHITECT Syphilis TP test plus 30 µL for each additional ARCHITECT Syphilis TP test from the same sample cup.
- > 3 hours on board: additional sample volume is required. For information on sample evaporation and volumes, refer to the ARCHITECT System Operations Manual, Section 5.
- If using primary or aliquot tubes, use the sample gauge to ensure sufficient patient specimen is present.

- Prepare calibrator and controls.
  - Mix ARCHITECT Syphilis TP Calibrator and Controls by gentle inversion before use.
  - To obtain the recommended volume requirements for the ARCHITECT Syphilis TP Calibrator and Controls, hold the bottles **vertically** and dispense 5 drops of calibrator or 5 drops of each control into each respective sample cup.
- Load samples.
  - For information on loading samples, refer to the ARCHITECT System Operations Manual, Section 5.
- Press RUN.
- For additional information on principles of operation, refer to the ARCHITECT System Operations Manual, Section 3.
- For optimal performance, it is important to perform routine maintenance as described in the ARCHITECT System Operations Manual, Section 9. Perform maintenance more frequently when required by laboratory procedures.

Specimen Dilution Procedures

Specimens cannot be diluted for the ARCHITECT Syphilis TP assay.

Calibration

- To perform an ARCHITECT Syphilis TP calibration, test Calibrator 1 in replicates of three. A single sample of each ARCHITECT Syphilis TP Control must be tested to evaluate the assay calibration. Ensure that assay control values are within the S/CO ranges specified in the control package insert. Calibrator 1 should be priority loaded.
- Once an ARCHITECT Syphilis TP calibration is accepted and stored, all subsequent samples may be tested without further calibration unless one or both of the following occur:
  - A reagent kit with a new lot number is used.
  - Controls are out of range.
- For detailed information on how to perform an assay calibration, refer to the ARCHITECT System Operations Manual, Section 6.

QUALITY CONTROL PROCEDURES

The recommended control requirement for the ARCHITECT Syphilis TP assay is that a single sample of each control be tested once every 24 hours each day of use for each reagent lot. If the quality control procedures in your laboratory require more frequent use of controls to verify test results, follow your laboratory-specific procedures. Ensure that assay control values are within the acceptable ranges specified in the control package insert. If a control is out of its specified range, the associated test results are invalid and must be retested. Recalibration may be indicated.

Verification of Assay Claims

For protocols to verify package insert claims, refer to the ARCHITECT System Operations Manual, Appendix B.

RESULTS

The ARCHITECT *i* System calculates the cutoff (CO) using the mean chemiluminescent signal (RLU) from three replicates of the Calibrator 1 and stores the result.

Calculation

The ARCHITECT Syphilis TP assay calculates a result based on a cutoff determined by the following calculation.

- Cutoff (CO) = Calibrator 1 Mean RLU x 0.20
- S/CO = Sample RLU / Cutoff RLU
- The cutoff RLU is stored for each reagent lot calibration.

Interpretation of Results

- Specimens with S/CO values < 1.0 are considered nonreactive by the ARCHITECT Syphilis TP assay.
- Specimens with S/CO values ≥ 1.0 are considered reactive by the ARCHITECT Syphilis TP assay.

Flags

- Some results may contain information in the Flags field. For a description of the flags that may appear in this field, refer to the ARCHITECT System Operations Manual, Section 5.

LIMITATIONS OF THE PROCEDURE

- False positive results can be expected with any test kit. The proportion of these falsely reactive specimens is dependent upon the specificity of the test kit, specimen integrity, and the characteristics of the local population being screened.
- If the ARCHITECT Syphilis TP results are inconsistent with clinical evidence, additional testing is suggested to confirm the result.
- No diagnostic test provides absolute assurance that a sample does not contain low levels of antibodies to TP, such as those present at a very early stage of infection. Therefore, a negative result at any time does not preclude the possibility of exposure to infection with syphilis. Additional information may be required for diagnosis.

SPECIFIC PERFORMANCE CHARACTERISTICS

Precision

The ARCHITECT Syphilis TP assay precision is ≤ 15% for the positive control. Precision was determined as described in the National Committee for Clinical Laboratory Standards (NCCLS) Protocol EP5-A2.[6] Six samples consisting of four serum based panels and both of Syphilis TP Controls were assayed in replicates of two at two separate times per day for twenty days (n=80 for each sample), using three lots of reagents. Data from this study are summarized in the following table.*

ARCHITECT Syphilis TP Precision

		Mean	Repeatability		Within-laboratory	
Sample	Lot	(S/CO)	SD	%CV	SD	%CV
Negative Control	1	0.09	0.0028	3.1	0.0052	5.8
	2	0.09	0.0024	2.7	0.0080	8.8
	3	0.08	0.0026	3.3	0.0062	7.7
Positive Control	1	2.53	0.059	2.3	0.094	3.7
	2	2.48	0.097	3.9	0.134	5.4
	3	2.49	0.114	4.6	0.127	5.1
Panel 1	1	6.13	0.200	3.1	0.294	4.8
	2	6.59	0.241	3.7	0.330	5.0
	3	6.49	0.173	2.7	0.293	4.5
Panel 2	1	3.20	0.100	3.1	0.143	4.5
	2	3.37	0.098	2.9	0.154	4.6
	3	3.30	0.141	4.3	0.196	5.9
Panel 3	1	1.54	0.095	6.1	0.133	7.3
	2	1.60	0.068	4.3	0.101	6.3
	3	1.63	0.063	3.9	0.083	5.1
Panel 4	1	0.74	0.033	4.4	0.042	5.6
	2	0.79	0.032	4.1	0.040	5.0
	3	0.80	0.041	5.2	0.045	5.6

* Representative data; results in individual laboratories may vary from these data.

Specificity

- The ARCHITECT Syphilis TP assay demonstrated a specificity of ≥ 99.0% in a study testing serum and plasma specimens from the following population:
  - Randomly selected blood donors (BD)
  - Randomly selected hospitalized patients (HP)

The testing was performed at two clinical sites and one internal site. Of 1800 BD specimens, 4 specimens were confirmed falsely reactive by ARCHITECT Syphilis TP assay, after a resolution using TPPA and FTA-ABS or other confirmatory techniques. Of 696 HP specimens, 2 specimens were confirmed falsely reactive by ARCHITECT Syphilis TP assay, after a resolution using TPPA and FTA-ABS or other confirmatory techniques. The data from this study are summarized in the following table.*

Specificity Results Using Random Blood Donors and Hospitalized Patients

Population	n	False Reactive	Specificity (%)
BD	1800	4	99.78
HP	696	2	99.71
Total	2496	6	99.76

* Representative data; results in individual laboratories may vary from these data.

Sensitivity

- The ARCHITECT Syphilis TP assay demonstrated a sensitivity of ≥ 99.0% in a study testing samples that were concordantly positive in TPPA, or were confirmed as true positive after resolution of discordants by FTA-ABS or other confirmatory data. The data from this study are summarized in the following table.*

Sensitivity Result

n	Reactive	Nonreactive	Observed Sensitivity
131	131	0	100.0%

* Representative data; results in individual laboratories may vary from these data.

Interference

Potential interference from elevated levels of triglycerides, bilirubin, protein and hemoglobin in the ARCHITECT Syphilis TP assay is < 0.4 S/CO difference on negative specimens and < 20% S/CO difference on positive samples with the following concentrations.

Test Compound	Test Concentration
Triglycerides	3000 mg/dL
Bilirubin	20 mg/dL
Protein	12 g/dL
Hemoglobin	500 mg/dL

BIBLIOGRAPHY

1. Meyer JC. Laboratory Diagnosis of Syphilis. *Curr Probl Dermatol.* 1996; 24: 1-11.
2. US Department of Labor, Occupational Safety and Health Administration, 29 CFR Part 1910.1030, Bloodborne pathogens.
3. US Department of Health and Human Services. *Biosafety in Microbiological and Biomedical Laboratories.* 5th ed. Washington, DC: US Government Printing Office, January 2007.
4. World Health Organization. *Laboratory Biosafety Manual.* 3rd ed. Geneva: World Health Organization; 2004.
5. Clinical and Laboratory Standards Institute. *Protection of Laboratory Workers from Occupationally Acquired Infections: Approved Guideline - Third Edition.* CLSI Document M29-A3. Wayne, PA: Clinical and Laboratory Standards Institute, 2005.
6. NCCLS. *Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline-Second Edition.* NCCLS document EP5-A2 (ISBN 1-56238-542-9). NCCLS, 940 West Valley Road, Suite 1400, Wayne, Pennsylvania 19087-1898 USA, 2004.

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