SIEMENS

ADVIA Centaur® XP
ADVIA Centaur® XPT
Immunoassay Systems

Syphilis (SYPH)

Current revision and date[a]	Rev. K, 2020-08	
Product Name	ADVIA Centaur® SYPH assay	**REF** 10492493
Systems	ADVIA Centaur XP system ADVIA Centaur XPT system	
Materials Required but Not Provided	ADVIA Centaur SYPH Quality Control ADVIA Centaur Ancillary Probe Wash 1 ADVIA Centaur Wash 1 (2 x 1500 mL) ADVIA Centaur Wash 1 (2 x 2500 mL)	**REF** 10492616 **REF** 03395373 **REF** 01137199 (112351) **REF** 03773025
Specimen Types	Human serum and plasma (EDTA, lithium-heparin, sodium-heparin, citrate)	
Reagent Storage	2–8°C	
Sample Volume	100 µL	
Calibration Interval	21 days	
Reagent On-System Stability	60 days	

[a] In Rev. B or later, a vertical bar in the margin indicates a technical update to the previous version.

WARNING
The ADVIA Centaur SYPH assay is not intended for blood and tissue donor screening. United States federal law restricts this device to sale by or on the order of a physician.

Intended Use

The ADVIA Centaur® Syphilis (SYPH) assay is an *in vitro* diagnostic immunoassay for the qualitative determination of antibodies to *Treponema pallidum* in human serum or plasma (EDTA, lithium or sodium heparinized, citrate) using the ADVIA Centaur® XP and ADVIA Centaur® XPT systems as an aid in the diagnosis of syphilis.

Summary and Explanation

The ADVIA Centaur SYPH assay is a direct sandwich immunoassay used for the detection of *Treponema pallidum* antibodies in human serum or plasma.

Syphilis is primarily transmitted via sexual contact, but can also be transmitted from mother to fetus. Syphilis is caused by the spirochete *T. pallidum*, which has never been successfully cultured in artificial media. Syphilis infections are classified into early (infectious) and late (non-infectious) stages. Early syphilis may be further divided into primary, secondary, and early latent syphilis. The signs and symptoms of syphilis are numerous; before the advent of serological testing, precise diagnosis was very difficult. In fact, the disease was often confused with other diseases, particularly in its tertiary stage. If not treated, syphilis can cause serious effects such as damage to the heart, aorta, brain, eyes, and bones. In some cases, these effects can be fatal. Therefore, the serological diagnosis of syphilis is very important.[1,2]

The serological diagnosis of syphilis is classified into two groups: nontreponemal tests and treponemal tests. Nontreponemal tests, which include venereal disease research laboratory (VDRL) and rapid plasma reagin (RPR) tests, detect antibodies formed by the host in response to lipid material released from damaged host cells as well as to lipoprotein-like material released from the spirochete. Treponemal tests detect specific treponemal antibodies, and the techniques used include agglutination (*T. pallidum* hemagglutination (TPHA), *T. pallidum* particle agglutination (TPPA), immunoassay (enzyme immunoassay [EIA] or chemiluminescent immunoassay [CLIA], immunofluorescence (fluorescent treponemal antibody absorption [FTA-ABS]), and immunoblotting. Nontreponemal tests have poor sensitivity and specificity, and recombinant antigen-based treponemal tests have higher sensitivity and specificity than native antigen-based treponemal tests.[3,4,5]

Principles of the Procedure

The ADVIA Centaur SYPH assay is intended to be a fully automated, antigen sandwich assay, using direct chemiluminometric technology. The ancillary pack reagent containing acridinium-ester-labeled *T. pallidum* recombinant antigens is added to the sample. These *T. pallidum* recombinant antigens complex with the antibodies in the sample. The solid phase reagent, containing biotinylated *T. pallidum* recombinant antigens preformed to streptavidin-coated magnetic latex particles, is then added to the sample. Antibody-antigen complexes will form if syphilis antibodies are present in the sample. The particles capture the *T. pallidum* recombinant antigen-antibody complexes.

Reagents

Reagent	Description	Storage	Reagent Stability
ADVIA Centaur SYPH ReadyPack® primary reagent pack; Solid Phase Reagent	20.0 mL/reagent pack: Streptavidin-coated paramagnetic microparticles preformed with biotinylated recombinant Tp15 antigen (~1.35 µg/mL) and biotinylated recombinant Tp17 antigen (~1.65 µg/mL) in buffer with surfactant, bovine gamma globulin, goat serum, and preservative	2–8°C	**Unopened:** Stable until the expiration date on the carton **On-system:** 60 days
ADVIA Centaur SYPH ReadyPack primary reagent pack; Ancillary Reagent	10.0 mL/reagent pack: Recombinant Tp15 antigen (~0.1 µg/mL) and recombinant Tp17 antigen (~0.15 µg/mL) labeled with acridinium esters in buffer with surfactant, goat serum, and preservative	2–8°C	**Unopened:** Stable until the expiration date on the carton **On-system:** 60 days

Reagent	Description	Storage	Reagent Stability
ADVIA Centaur SYPH Calibrator	2.0 mL/vial Human plasma positive for *Treponema pallidum* antibodies in phosphate buffer with sodium azide (< 0.1%)	2–8°C	**Unopened:** Stable until the expiration date on the vial **On-system:** 8 hours
ADVIA Centaur ReadyPack ancillary reagent pack; Ancillary Probe Wash 1[a] APW 1	25.0 mL/pack 0.4 N sodium hydroxide	2–8°C	**Unopened:** Stable until the expiration date on the pack **On-system:** 14 days
ADVIA Centaur Wash 1[a] WASH 1	1500 mL/pack Phosphate-buffered saline with sodium azide (< 0.1%) and surfactant	2–25°C	**Unopened:** Stable until the expiration date on the pack **On-system:** 1 month
ADVIA Centaur Wash 1[a] WASH 1	2500 mL/pack Phosphate-buffered saline with sodium azide (< 0.1%) and surfactant	2–25°C	**Unopened:** Stable until the expiration date on the pack **On-system:** 1 month

a See *Materials Required but Not Provided*

Warnings and Precautions

Safety data sheets (MSDS/SDS) available on siemens.com/healthcare.

CAUTION POTENTIAL BIOHAZARD

Each donation of human blood or blood component was tested by FDA-approved methods for the presence of antibodies to human immunodeficiency virus type 1 (HIV-1) and type 2 (HIV-2), as well as for hepatitis B surface antigen (HBsAg) and antibody to hepatitis C virus (HCV). The test results were negative (not repeatedly reactive). No test offers complete assurance that these or other infectious agents are absent; this material should be handled using good laboratory practices and universal precautions.[6–8]

Some components of this product contain human source material. No known test method can offer complete assurance that products derived from human blood will not transmit infectious agents. All products manufactured using human source material should be handled as potentially infectious. Handle this product according to established good laboratory practices and universal precautions.[6–8]

The negative control has been assayed by FDA-approved methods and found to be nonreactive for antibodies to *T. pallidum*, hepatitis B surface antigen, antibody to HCV, and antibody to HIV-1/2. The positive control has been assayed by FDA-approved methods and found to be nonreactive for hepatitis B surface antigen, antibody to HCV, and antibody to HIV-1/2. The positive control, low calibrator, and high calibrator contain human plasma that is reactive for antibody to *T. pallidum*. All products manufactured using human source material should be handled as potentially infectious.

CAUTION

This device contains material of animal origin and should be handled as a potential carrier and transmitter of disease.

Contains sodium azide as a preservative. Sodium azide can react with copper or lead plumbing to form explosive metal azides. On disposal, flush reagents with a large volume of water to prevent buildup of azides. Disposal into drain systems must be in compliance with prevailing regulatory requirements.

H319, H315, H290 Warning!

P280, P264, P305+P351+P338 Causes serious eye irritation. Causes skin irritation. May be corrosive to metals. Wear protective gloves/protective clothing/eye protection/face protection. Wash hands thoroughly after handling. IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.

Contains: sodium hydroxide; ADVIA Centaur Ancillary Probe Wash 1

Dispose of hazardous or biologically contaminated materials according to the practices of your institution. Discard all materials in a safe and acceptable manner and in compliance with prevailing regulatory requirements.

For *in vitro* diagnostic use.

Preparing Reagents

All reagents are liquid and ready to use.

Remove all of the reagents from the refrigerator and mix all primary reagent packs by hand before loading them onto the system. Visually inspect the bottom of the reagent pack to ensure that all particles are dispersed and resuspended. For detailed information about preparing the reagents for use, see the system operating instructions.

Note The Ancillary Reagent provided in this kit is matched to the ReadyPack primary reagent pack. Do not mix Ancillary Reagent lots with different lots of reagent packs.

Note

- Discard reagent packs at the end of the 60-day onboard stability interval.
- Do not use reagents beyond the expiration date.

Storing and Stability

Store the reagents upright at 2–8°C.

Protect reagent packs from all heat and light sources. Reagent packs loaded on the system are protected from light. Store unused reagent packs at 2–8°C away from heat and light sources.

All reagents are stable at 2–8°C until the expiration date on the packaging.

Specimen Collection and Handling

Serum, EDTA plasma, lithium or sodium heparinized plasma, citrate plasma are the recommended sample types for this assay.

The following recommendations for handling and storing blood samples are furnished by the Clinical and Laboratory Standards Institute (CLSI),[9] and augmented with additional sample handling studies using the ADVIA Centaur SYPH assay:

- Handle all samples as if capable of transmitting disease.
- Samples are processed by centrifugation, typically followed by physical separation of the serum or plasma from the red cells. The centrifugation step may occur up to 24 hours post-draw. When testing 10 samples where the centrifugation step was varied up to 24 hours post-draw, no clinically significant differences were observed.
- Test samples as soon as possible after collecting.

Store specimens according to the following recommendations:

- Store samples at 2–8°C if not tested immediately.
- Store primary tube samples at 2–8°C up to 7 days. Keep samples stoppered at all times. Primary tube samples include serum stored on the clot, plasma stored on packed red cells, and samples processed and stored in gel barrier blood collection tubes. When 10 samples in these primary tubes were tested up to 7 days, no clinically significant differences were observed.
- Freeze samples, devoid of red blood cells, at or below -20°C for longer storage. Do not store in a frost-free freezer. Thoroughly mix thawed samples and centrifuge before using. When 10 samples were subject to 6 freeze/thaw cycles, no clinically significant differences were observed.

- Package and label samples for shipment in compliance with applicable federal and international regulations covering the transport of clinical samples and etiological agents. Store samples stoppered at 2–8°C upon arrival. If shipment is expected to exceed 7 days, ship specimens frozen. Samples maintained at room temperature up to 7 days or refrigerated up to 7 days demonstrated no qualitative differences.

The purpose of handling and storage information is to provide guidance to users. It is the responsibility of the individual laboratory to use all available references and/or its own studies when establishing alternate stability criteria to meet specific needs.

Procedure

Materials Provided

The following materials are provided:

REF	Contents	Number of Tests
10492493	1 ReadyPack primary reagent pack containing ADVIA Centaur SYPH Solid Phase Reagent 1 Ancillary pack containing ADVIA Centaur SYPH Ancillary Reagent ANC 2 vials ADVIA Centaur SYPH low calibrator CAL L 2 vials ADVIA Centaur SYPH high calibrator CAL H ADVIA Centaur and ADVIA Centaur CP SYPH Master Curve card ADVIA Centaur and ADVIA Centaur CP SYPH Calibrator Assigned Value cards	200

Materials Required but Not Provided

The following materials are required to perform this assay, but are not provided:

Item	Description	
REF 10492616	ADVIA Centaur SYPH quality control material	2 x 7.0 mL negative control CONTROL – 2 x 7.0 mL positive control CONTROL + Expected Value card
REF 03395373	ADVIA Centaur Ancillary Probe Wash 1 APW 1	2 ReadyPack ancillary reagent packs containing 25.0 mL per pack
REF 01137199 (112351)	ADVIA Centaur Wash 1 WASH 1	2 x 1500 mL/pack
REF 03773025	ADVIA Centaur Wash 1 [a] WASH 1	2 x 2500 mL/pack

a for use with systems with 2500 mL capacity

Assay Procedure

For detailed instructions on performing the procedure, refer to the system operating instructions.

The ADVIA Centaur XP and ADVIA Centaur XPT system automatically perform the following steps:

1. Dispenses 100 µL of sample into a cuvette.
2. Dispenses 40 µL of Ancillary Pack Reagent and incubates for 5 minutes at 37°C.
3. Dispenses 100 µL of Solid Phase and incubates the mixture for 18 minutes at 37°C.
4. Separates the Solid Phase from the mixture and aspirates the unbound reagent.

5. Washes the cuvette with Wash 1.
6. Dispenses 300 µL each of Acid Reagent and Base Reagent to initiate the chemiluminescent reaction.

A direct relationship exists between the level of antibodies to *T. pallidum* present in the patient sample and the amount of relative light units (RLUs) detected by the system. A result of reactive, nonreactive, or equivocal is determined according to the Index Value established with the calibrators. Refer to *Interpretation of Results* for a description of the cut-off value calculation.

The ADVIA Centaur systems report results according to the selected option, as described in the system operating instructions.

Note If a system error occurs, and the rocking of the primary reagent compartment is stopped for more than 5 minutes, remove and mix the ADVIA Centaur SYPH ReadyPack primary reagent packs until the particles are in solution before loading onto the system.

Preparing the System

For detailed information about preparing the system, refer to the system operating instructions.

Ensure that the system has sufficient primary and ancillary reagent packs. Load the primary reagent packs in the primary reagent area. You can use the arrows on the end label as a placement guide. The system automatically mixes the primary reagent packs to maintain homogeneous suspension of the reagents. Load the ancillary reagent packs in the ancillary reagent entry. For detailed information about loading reagents, refer to the system operating instructions.

Preparing the Samples

This assay requires 100 µL of sample for a single determination. This volume does not include the unusable volume in the sample container or the additional volume required when performing duplicates or other tests on the same sample. For detailed information about determining the minimum required volume, see the system operating instructions.

Before placing samples on the system, ensure that samples have the following characteristics:

- Samples are free of fibrin or other particulate matter. Remove particulates by centrifugation.
- Samples are free of bubbles or foam.

On-System Stability

The ADVIA Centaur SYPH assay reagents are stable unopened until the expiration date on the carton or onboard the system for 60 days.

Performing Calibration

For calibration of the ADVIA Centaur SYPH assay, use ADVIA Centaur SYPH Calibrators provided with each kit. The calibrators provided in this kit are matched to the ReadyPack primary and ancillary reagent packs. Do not mix calibrator lots with different lots of reagent packs.

Each calibrator is packaged with a lot-specific Calibrator Assigned Value card to facilitate entering the calibration values on the system. Enter the values using the bar-code scanner or the keyboard. For detailed information about entering calibrator values, refer to the system operating instructions.

Perform the calibration procedure using the following steps:

Note This procedure uses calibrator volumes sufficient to measure each calibrator in duplicate.

1. Schedule the calibrators to the worklist.
2. Label 2 sample cups with calibrator bar-code labels: one cup for the low calibrator and another cup for the high calibrator.
3. Gently mix the low and high calibrators and dispense at least 9–10 drops of each calibrator into the appropriate sample cups. Avoid bubbles.

   Note Each drop from the calibrator vial is approximately 50 µL.
4. Load the sample cups in a rack.
5. Place the rack in the sample entry queue.
6. Ensure that the assay reagents are loaded.
7. Start the entry queue, if required.

Note Dispose of any calibrator remaining in the sample cups after 8 hours. Do not refill sample cups when the contents are depleted; if required, dispense fresh calibrators.

Calibration Frequency

Calibrate the assay at the end of the 21-day calibration interval.

Additionally, the ADVIA Centaur SYPH assay requires a two-point calibration when:

- Changing lot numbers of primary reagent packs.
- Replacing system components.
- Quality control results are repeatedly out of range.

Using Bar-Code Labels

Calibrator bar-code labels are lot-number specific. Do not use bar-code labels from one lot of calibrators with any other lot of calibrators.

Use the ADVIA Centaur SYPH Calibrator bar-code labels to identify the Low and High Calibrator sample cups when performing the ADVIA Centaur SYPH assay. Place the bar-code label on the sample cup so that the readable characters on the side of the label are vertical on the sample cup.

Performing Master Curve Calibration

The ADVIA Centaur SYPH assay requires a Master Curve calibration when using a new lot number of Solid Phase and Ancillary Pack Reagents. For each new lot number of Solid Phase and Ancillary Pack Reagents, use the bar-code reader or keyboard to enter the Master Curve values on the system. The Master Curve card contains the Master Curve values. For detailed information about entering calibration values, refer to the system operating instructions.

Performing Quality Control

Follow government regulations or accreditation requirements for quality control frequency.

To monitor system performance and chart trends, as a minimum requirement, quality control materials with at least two levels (low and high) of *T. pallidum* should be assayed on each day that samples are analyzed. Quality control samples should also be assayed when performing a two-point calibration. Treat all quality control samples the same as patient samples.

For quality control of the ADVIA Centaur SYPH assay, use ADVIA Centaur SYPH quality control materials. Refer to the Expected Value card for the suggested expected values specific for the lot number of the positive and negative controls.

For detailed information about entering quality control values, refer to the system operating instructions.

Perform the quality control procedure using the following steps:

Note This procedure uses control volumes sufficient to measure each control in duplicate.

1. Schedule the quality control samples to the worklist.
2. Label 2 sample cups with quality control bar-code labels: one cup for the positive control, and another cup for the negative control.
3. Gently mix the quality control materials and dispense at least 9–10 drops of each control into the appropriate sample cups. Avoid bubbles.

   Note Each drop from the control vial is approximately 50 mL.
4. Load the sample cups in a rack.
5. Place the rack in the sample entry queue.
6. Ensure that the assay reagents are loaded.
7. Start the entry queue, if required.

Note Dispose of any quality control materials remaining in the sample cups after 8 hours. Do not refill sample cups when the contents are depleted; if required, dispense fresh quality control materials.

Using Bar-Code Labels

Control bar-code labels are lot-number specific. Do not use bar-code labels from one lot of controls with any other lot of controls.

Use the ADVIA Centaur SYPH quality control bar-code labels to identify the positive and negative sample cups when performing the ADVIA Centaur SYPH assay. Place the bar-code label on the sample cup so that the readable characters on the side of the label are vertical on the sample cup.

Taking Corrective Action

If the quality control results do not fall within the Expected Values or within the laboratory's established values, do not report results. Take the following actions:

1. Determine and correct the cause of the unacceptable control results:
   a. Verify that the materials are not expired.
   b. Verify that required maintenance was performed.
   c. Verify that the assay was performed according to the instructions for use.
   d. Rerun the assay with fresh quality control samples, and confirm that quality control results are within acceptable limits before running patient samples.
   e. If the quality control results are not within acceptable limits, recalibrate the assay, and repeat step d.
   f. If necessary, contact your local technical support provider or distributor for assistance.
2. Repeat testing of patient samples before reporting results.

Perform corrective actions in accordance with your established laboratory protocol.

Results

Calculation of Results

For detailed information about how the system calculates results, refer to the system operating instructions.

The ADVIA Centaur systems report results according to the selected option, as described in the system operating instructions.

The system reports SYPH results in Index Values and as reactive, equivocal, or nonreactive.

Interpretation of Results

Results should always be interpreted in conjunction with the patient's medical history, clinical presentation, and other findings.

The system reports syphilis results as nonreactive, equivocal, or reactive, based on index values established with the calibrators:

- Samples with an Index Value < 0.90 are considered nonreactive for syphilis *T. pallidum* antibodies.
- Samples with an Index Value ≥ 0.90 and < 1.10 are considered equivocal.
- Samples with an Index Value ≥ 1.10 are considered reactive for syphilis *T. pallidum* antibodies.

If the controls are out of range, specimen results are invalid and must be repeated.

Samples with equivocal values should be retested in duplicate:

- If 2 out of 3 results are < 0.90 Index, the sample is considered nonreactive.
- If 2 out of 3 results are ≥ 1.10 Index, the sample is considered reactive.
- If 2 of the 3 sample results remain equivocal, supplemental testing of the sample is recommended.

The cutoff for the ADVIA Centaur SYPH assay was verified based on results of a receiver-operating characteristic (ROC) curve.[10]

Limitations

The following information pertains to limitations of the assay:

- The ADVIA Centaur SYPH assay is limited to the detection of antibodies to *T. pallidum* in human serum or plasma (EDTA, lithium or sodium heparinized plasma, citrated plasma).
- A nonreactive test result does not exclude the possibility of exposure to or infection with syphilis. *T. pallidum* antibodies may be undetectable in some stages of the infection and in some clinical conditions.
- Assay performance characteristics have not been established when the ADVIA Centaur SYPH assay is used in conjunction with other manufacturers' assays for specific syphilis serological markers.
- The performance of the ADVIA Centaur SYPH assay has not been established with neonatal specimens, cadaver specimens, heat-inactivated specimens, or body fluids other than serum or plasma, such as saliva, urine, amniotic, or pleural fluids.
- Assay interference due to possible circulating antibodies against pinta, yaws, and leptospirosis has not been evaluated.
- As with any chemical reaction, you must be alert to the possible effect on results of unknown interferences from medications or endogenous substances. The laboratory and physician must evaluate all patient results in light of the total clinical status of the patient.
- Do not use specimens with obvious microbial contamination.

Expected Values

A population of 806 apparently healthy male and female subjects [including pregnant (332), pediatric (75), and adult/not pregnant (399)] were tested using the ADVIA Centaur SYPH assay. Of these samples, 5 (0.6%) were reactive, 0 (0.0%) were equivocal, and 801 (99.4%) were nonreactive.

As with all *in vitro* diagnostic assays, each laboratory should determine its own reference range(s) for the diagnostic evaluation of patient results.[11]

Performance Characteristics

Precision

The ADVIA Centaur SYPH assay is designed to have a Within-Run precision CV(%) and a Total CV(%) as described in the table below.

Precision was evaluated according to the CLSI protocol EP5-A2.[12] According to this protocol, the assay was run 2 times per day for 20 days (n = 80 per sample) using 1 reagent lot. The instrument was calibrated on the first run of day one and recalibrated at the recommended calibration interval. Assay results were calculated using a two-point calibration. The following results were obtained:

Sample	Number of Replicates	Mean Index	Within-Run		Within-Run Designed to be ≤	Between-Run		Between-Day		Total		Total Designed to be ≤
			SD	CV(%)	CV(%)	SD	CV(%)	SD	CV(%)	SD	CV(%)	CV(%)
Control Negative (plasma, low negative)	80	0.11	0.00	NA[a]	NA	0.00	NA	0.00	NA	0.01	NA	NA
Control Positive (plasma, moderate positive)	80	3.84	0.06	1.50	8	0.04	0.99	0.12	3.22	0.14	3.69	10
Plasma pool (moderate positive)	80	1.99	0.03	1.44	8	0.02	1.05	0.06	2.93	0.07	3.43	10
Serum pool 1 (low negative)	80	0.19	0.00	NA	NA	0.00	NA	0.00	NA	0.01	NA	NA
Serum pool 2 (high negative)	80	0.80	0.01	1.16	10	0.01	0.86	0.02	2.86	0.03	3.20	12
Serum pool 3 (low positive)	80	1.28	0.02	1.31	10	0.01	0.93	0.04	2.79	0.04	3.22	12
Serum pool 4 (high positive)	80	6.96	0.10	1.45	8	0.07	0.95	0.25	3.63	0.28	4.02	10
Serum pool 5 (high positive)	80	21.45	0.41	1.93	8	0.28	1.29	0.75	3.50	0.90	4.20	10

[a] NA = Not Applicable

Assay results obtained at individual laboratories may vary from the data presented.

Assay Reproducibility

A reproducibility study was conducted using two reagent lots at three external sites. The protocol was run over 10 days, 2 runs per day, and 4 replicates per run for the sample pools, and 8 replicates per run for the negative and positive control materials. Reproducibility data was pooled across 3 sites, and data is presented for a representative reagent lot.

			Within-Run		Between-Run		Between-Day		Total	
Sample	Number of Replicates	Mean Index	SD	CV(%)	SD	CV(%)	SD	CV(%)	SD	CV(%)
Control Negative (plasma, low negative)	480	0.11	0.00	NA[a]	0.00	NA	0.01	NA	0.01	NA
Control Positive (plasma, moderate positive)	480	3.56	0.06	1.6	0.04	1.2	0.05	1.4	0.09	2.5
Serum pool 1 (low negative)	240	0.18	0.00	NA	0.00	NA	0.01	NA	0.01	NA
Serum pool 2 (high negative)	240	0.75	0.01	1.3	0.01	1.4	0.01	1.3	0.02	2.3
Serum pool 3 (low positive)	240	1.20	0.02	1.5	0.02	1.4	0.01	1.2	0.03	2.4
Serum pool 4 (high positive)	240	6.67	0.10	1.5	0.11	1.6	0.08	1.2	0.17	2.5
Serum pool 5 (high positive)	240	20.42	0.29	1.4	0.31	1.5	0.31	1.5	0.53	2.6

a NA = Not Applicable

Accuracy / Method Comparison

Percent agreement was determined by comparing the performance of the ADVIA Centaur SYPH assay to commercially available syphilis assays. A total of 2108 samples were tested on the ADVIA Centaur system, split between 2 different test lots, including the following specimens:

- 474 apparently healthy subjects (including pediatrics)
- 285 medically-diagnosed syphilis samples
- 124 samples reactive by previous laboratory testing (treponemal and non-treponemal methods)
- 370 samples sent for routine syphilis testing
- 339 samples from pregnant subjects
- 516 HIV-positive samples

Equivocal samples were repeated in singlicate on the instrument that gave the equivocal results. If a sample reported an equivocal result upon retesting, the sample result was reported as equivocal; otherwise, the sample was retested a third time in singlicate to assign a 2-out-of-3-rule outcome.

For purposes of percent agreement calculations, equivocal results obtained on the ADVIA Centaur system (n = 4) were assigned the opposite clinical interpretation of the comparative assay result. Equivocal results obtained on the comparative system (n = 2) were removed from the analysis.

Percent Agreement: Total Study Population

The negative percent agreement of the ADVIA Centaur SYPH assay compared to the comparative assay was 99.4% (1382/1391) with a 95% confidence interval (CI) of 98.8–99.7%.

The positive percent agreement of the ADVIA Centaur SYPH assay compared to the comparative assay was 97.9% (700/715) with a 95% confidence interval (CI) of 96.6–98.8%.

	Comparative Assay			
ADVIA Centaur System	**Reactive**	**Indeterminate**	**Nonreactive**	**Total**
Reactive	700	1	6	707
Equivocal	1	0	3	4
Nonreactive	14	1	1382	1397
Total	**715**	**2**	**1391**	**2108**

Percent Agreement: Apparently Healthy Population

A population of 806 apparently healthy subjects was tested using the ADVIA Centaur SYPH assay and a commercially available syphilis assay. The performance of the ADVIA Centaur SYPH assay is shown in the following table:

Apparently Healthy Subjects	Reactive	Equivocal	Nonreactive	Total	Negative Percent Agreement
Pregnant	1 (0.3%)	0 (0.0%)	331 (99.7%)	332	100% (329/329)
Pediatric	1 (1.3%)	0 (0.0%)	74 (98.7%)	75	100% (73/73)
Other[a]	3 (0.8%)	0 (0.0%)	396 (99.2%)	399	100% (389/389)
Total	**5 (0.6%)**	**0 (0.0%)**	**801 (99.4%)**	**806**	**100% (791/791)**

a Other refers to samples from apparently healthy adults who are not pregnant.

Percent Agreement: Expected Positive Population

Samples from patient populations expected to test positive for syphilis were tested on the ADVIA Centaur and on a commercially available syphilis assay. These samples were from subjects found reactive by previous laboratory testing, and subjects who had been medically diagnosed with syphilis.

The positive percent agreement of the ADVIA Centaur SYPH assay to the comparative assay was 99.4% (535/538) with a 95% confidence interval (CI) of 98.4–99.9%.

Expected Positive Subjects	Reactive	Equivocal	Nonreactive	Total	Positive Percent Agreement
TPPA/RPR-Reactive	271 (98.2%)	1 (0.4%)	4 (1.4%)	276	99.6% (271/272)
Medically Diagnosed	264 (92.6%)	0 (0.0%)	21 (7.4%)	285	99.2% (264/266)
Total	**535 (95.4%)**	**1 (0.2%)**	**25 (4.5%)**	**561**	**99.4% (535/538)**

Percent Agreement: Intended Use Population

Samples from patient populations expected to receive routine testing for syphilis (samples sent for routine testing and HIV-positive samples) were tested on the ADVIA Centaur and on a commercially available syphilis assay.

The negative percent agreement of the ADVIA Centaur SYPH assay compared to the comparative assay was 98.4% (568/577) with a 95% confidence interval (CI) of 97.1–99.3%.

The positive percent agreement of the ADVIA Centaur SYPH assay compared to the comparative assay was 98.2% (160/163) with a 95% confidence interval (CI) of 94.7–99.6%.

	Comparative Assay			
ADVIA Centaur System	**Reactive**	**Indeterminate**	**Nonreactive**	**Total**
Reactive	160	1	6	167
Equivocal	0	0	3	3
Nonreactive	3	0	568	571
Total	**163**	**1**	**577**	**741**

Interferences

The ADVIA Centaur SYPH assay was evaluated for potential cross-reactivity with other viral infections, disease-state specimens, and other populations. The reactive syphilis status of each specimen was verified using a syphilis comparative assay. The following results were obtained using the ADVIA Centaur SYPH assay:

		Number of Reactive Anti-Syphilis Results	
Clinical Category	**Number Tested**	**ADVIA Centaur Assay**	**Comparative Assay**
Lyme Disease	10	1	1
Anti-Nuclear Antibody (ANA)	10	0	0
Rheumatoid Factor	10	0	0
HAMA	10	2	2
Hepatitis A Infection (HAV) Total	20	10	10
Hepatitis A Infection (HAV) IgM	5	0	0
Hepatitis B Infection (HBV)	10	0	0
Hepatitis C Infection (HCV)	10	0	0
Human Immunodeficiency Virus (HIV)	11	0	0
Cytomegalovirus (CMV) IgG	10	0	0
Cytomegalovirus (CMV) IgM	5	0	0
Epstein-Barr Virus (EBV) IgG	10	0	0
Herpes Simplex Virus (HSV) IgG	10	5	5
Rubella IgG	10	0	0
Rubella IgM	10	0	0
Toxoplasma IgG	10	1	1
Toxoplasma IgM	10	0	0
Varicella Zoster Virus (VZV) IgG	10	2	2
Systemic Lupus Erythematosus (SLE)	10	0	0
Drug users	20	3	3
Flu Vaccine recipients	26	0	0
Cord Blood	18	1	1
Pregnancy (1st, 2nd, and 3rd Trimesters)	74	2	2
Pediatrics	48	0	0
Hospitalized	51	2	2
Transplant Patients	20	0	0
High IgG	5	0	0
High IgM	10	0	0
Myeloma patients	13	0	1
Total Samples Tested	**476**	**29**	**30**

All samples that demonstrated a positive result (with the exception of two HAV-positive samples) were also confirmed positive by other tests (TPPA or RRP), indicating reactivity to Syphilis *(T. Pallidum* antibodies) rather than cross reactivity.

The ADVIA Centaur SYPH assay was evaluated for interference according to CLSI guideline EP7-A2.[13] The following substances were found not to interfere at the concentrations indicated. A bias less than 10% is not considered a significant interference:

Substance Tested	Test Concentration
Hemoglobin	500 mg/dL
Triglycerides (intralipids)	1000 mg/dL
Cholesterol	400 mg/dL
Bilirubin, conjugated	40 mg/dL
Bilirubin, unconjugated	40 mg/dL
Protein (human serum albumin)	11 g/dL
hyper-IgG	30 mg/mL

Specimens that contain biotin at a concentration of 3500 ng/mL demonstrate no change in interpretation. Biotin concentrations greater than this may lead to a change in interpretation.

Biotin (ng/mL)	Index		
	Nonreactive	Low Reactive	High Reactive
0	0.00	1.42	3.27
219	0.00	1.19	2.84
3500	0.00	1.21	2.80

Technical Assistance

For customer support, please contact your local technical support provider or distributor.

siemens.com/healthcare

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Definition of Symbols

The following symbols may appear on the product labeling:

Symbol	Definition	Symbol	Definition
IVD	*In vitro* diagnostic medical device	REF REF	Catalog number
	Legal manufacturer	EC REP	Authorized Representative in the European Community
CE	CE Mark	CE 0088	CE Mark with identification number of notified body
	Consult instructions for use		Biological risk
	Do not freeze (> 0°C)		Temperature limitation
	Lower limit of temperature		Upper limit of temperature
	Keep away from sunlight and heat	UP	Up
	Use by	Σ (n)	Contains sufficient for (n) tests
LOT	Batch code		Shake the reagent pack vigorously. Refer to *Preparing Reagents* in the assay-specific ADVIA Centaur product instructions for detailed information.
YYYY-MM-DD	Date format (year-month-day)	Rev.	Revision
MC DEF	Master Curve Definition	CHECKSUM	Variable hexadecimal number that ensures the Master Curve and Calibrator definition values entered are valid.
LOT DTL	Lot Details	DER GRÜNE PUNKT	Green dot
	Recycle	PRINTED WITH SOY INK	Printed with soy ink

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