Considerations for the Implementation of Point of Care (POC) Tests for Syphilis

National Syphilis and Congenital Syphilis Syndemic Federal Task Force

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DISCLAIMER

This document is developed by the National Syphilis and Congenital Syphilis Syndemic Federal Task Force for the Implementation of Point of Care Tests for Syphilis document which is designed to address the challenges in diagnosis and treatment of syphilis. It emphasizes the often-asymptomatic nature of the infection and discusses the implementation of Point of Care (POC) tests to facilitate rapid diagnosis and treatment during the same visit.

Purpose of the NSCSS Considerations for the Implementation of Point of Care Tests for Syphilis

POC tests for syphilis differs from the traditional laboratory-based serologic testing primarily in specimen collection, time to result, need for confirmation, and sensitivity/specificity. While POC tests offers rapid results using whole blood from a fingerstick, it lacks the comprehensive assessment provided by laboratory-based tests, requiring confirmation and follow-up. It also underscores that laboratory-based testing remains the preferred option, particularly for individuals with a history of syphilis and low-risk individuals. Despite lower sensitivity and specificity, POC tests can be valuable, especially in settings with high incidence rates or where access to healthcare is limited.

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For questions or comments, please email STI@hhs.gov

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National Syphilis and Congenital Syphilis Syndemic Federal Task Force Considerations for the Implementation of Point of Care Tests for Syphilis

Over the past decade, syphilis rates and case numbers in the U.S. have increased across all populations. Syphilis infection can be difficult to diagnose. People are often asymptomatic, which makes screening a crucial step in diagnosis. Most current syphilis testing in the U.S. is done through laboratory-based serologic (i.e., antibody) tests that need to be sent from the provider to a laboratory which can delay diagnosis and treatment. The Food and Drug Administration (FDA) has authorized many such laboratory-based serologic tests and has authorized two Clinical Laboratory Improvement Amendments (CLIA)-waived point-of-care (POC) tests for syphilis to detect antibodies to *Treponema pallidum.* The tests use whole blood, serum, or plasma from a fingerstick that can provide rapid test results during the same visit:

- Syphilis Health Check Treponemal Antibody Test (SHC) provides results in about 10-15 minutes.
- ChemBio DPP HIV-Syphilis (ChemBio DPP) detects HIV as well as syphilis in about 15 minutes.

Disclaimer:

- All references to POC tests in this document are strictly referring to the two FDA-authorized tests mentioned above. Any mention of POC tests should be interpreted as a reference to these two authorized tests only.
- All references to laboratory-based tests in this document are strictly referring to FDA-authorized tests. Any mention of laboratory-based tests should be interpreted as a reference to tests that comply with FDA standards and regulations.

How do syphilis POC tests differ from laboratory-based serologic syphilis tests?

There are four main differences in syphilis POC tests and laboratory-based serologic syphilis tests:

1. **Specimen Collection**. Syphilis POC tests typically use whole blood from a fingerstick, while laboratory-based serologic tests generally require venipuncture (i.e., blood draw).

2. **Time to Result**. Syphilis POC tests typically offer results in about 15 minutes. The time for laboratory-based serologic tests results generally vary from hours to weeks. The difference in time of the test results may influence how quickly treatment can be provided. These delays may require the patient to return to the clinic for treatment.

3. **Syphilis POC tests are generally used as an initial screening test or in conjunction with a non-treponemal laboratory test and clinical findings to aid in the diagnosis of syphilis infection**. Diagnosing syphilis relies on two different types of antibody tests used in combination – a treponemal-specific test and a nontreponemal test. Syphilis POC tests provide only treponemal results. Since treponemal tests generally remain positive for life after someone has had syphilis, they cannot differentiate between treated and untreated syphilis infections. Non-treponemal tests are reported quantitatively as titers. They are used in conjunction with a clinical and sexual history and physical exam to distinguish between older and more recent syphilis infections and monitor infection resolution over time. Results from syphilis POC tests are thus generally confirmed using confirmatory laboratory-based serologic tests.

4. **Syphilis POC tests generally have lower sensitivity and specificity**. Syphilis POC tests generally will produce more false negative results (infections will be missed) and more false positive results (positive result without an infection) when compared to laboratory-based serologic tests that combine both treponemal and nontreponemal test results. Table 1 provides general estimates of sensitivity and specificity of laboratory-based and POC tests.

Table 1. Performance Estimates^ for Syphilis Serologic Tests^^

Test Type		Sensitivity			Specificity
		Primary	Secondary	Latent	
Nontreponemal Tests	RPR	~85%	~100%	~95%	~99%
	VDRL	~75%	~100%	~95%	~99%
Treponemal Tests	TPPA	~95%	~100%	~100%	~99%
	EIA	~90%	~100%	~100%	~99%
POC Tests*	SHC	~96% (range 77%–100%)			~97%
	Chembio DPP	~90% (range 85%–100%)			~96%

EIA = enzyme immunoassay
RPR = rapid plasma reagin
TPPA = *Treponema pallidum* particle agglutination
VDRL = Venereal Disease Research Laboratory

^The performance of syphilis tests varies by the stage of syphilis. The performance estimates presented in this table are approximations because reference standards and participants from whom samples were collected varied between studies. For additional information, please refer to the CDC Laboratory Recommendations for Syphilis Testing, United States, 2024, (https://www.cdc.gov/mmwr/volumes/73/rr/rr7301a1.htm)

^^Serologic tests that measure antibodies to both nontreponemal and treponemal antigens related to syphilitic infections should be used in combination, when the primary test is reactive, to aid in the diagnosis of syphilis. Sole reliance on one reactive serologic test result can misclassify a patient's syphilis status.

*Performance estimates and ranges based on unpublished CDC metanalysis from limited published data. See references 1-8.

How can syphilis POC tests improve serologic syphilis testing and care?

When should laboratory-based tests be used? When should POC tests be used?

POC tests can be a useful component of a syphilis testing and treatment program, particularly for individuals who access health care infrequently and have difficulty with follow-up visits. In some settings and for some populations, the rapid results from a positive POC test create an opportunity to treat for syphilis during the same visit, based on clinical judgement. In general, POC tests should be used where syphilis rates are high. However, individuals previously treated for syphilis should have testing done with laboratory-based serologic tests, not POC tests.

Unique Features to Consider for a Syphilis POC Tests Program

- **Staffing**: POC tests generally can be conducted by trained non-clinical staff or clinicians. If present, clinical staff can reassure the test is read correctly, help evaluate patients with positive POC test results, and provide treatment at the same visit. When POC tests are performed outside a clinical setting, by non-clinical staff, quick referral and linkage to a clinical setting should be coordinated for those with positive results.
- **CLIA requirement**: The two authorized syphilis POC tests can be performed at a laboratory that holds a CLIA certificate of waiver. See Clinical Laboratory Improvement Amendments (CLIA) | CMS.
- **Training of testers:** Testers are encouraged to be trained and remain up to date on usage of the tests. When not testing routinely, testers must be re-certified. Testers need training on communicating the test results, especially for counseling about the uncertainty of the POC tests results and importance of follow-up.
- **Collaboration with the local health department**: Close collaboration through regularly scheduled meetings or telephone or secure email connection with local health department officials can enhance care, coordination, and follow-up. The health department can offer partner services.

- **Reporting recommendations**: It is recommended that POC and follow-up tests be reported to the local health department. If treatment was provided or pregnancy status is known, these should also be reported. Laboratories are required to report to state, local, and national public health authorities in accordance with applicable laws.
- **Reporting problems with a test to FDA**: Mandatory reporters (that is, manufacturers, device user facilities, and importers) are required to submit to the FDA certain types of reports for adverse events and product problems about medical devices. In addition, the FDA encourages health care professionals, patients, caregivers and consumers to submit voluntary reports about serious adverse events that may be associated with a medical device, as well as use errors, product quality issues, and therapeutic failures. These reports, along with data from other sources, can provide critical information that helps improve patient safety.

Managing POC Test Results

- **Positive Test**: All persons with positive tests should receive serologic confirmatory testing with a quantitative nontreponemal test and a second treponemal test. This requires a trained staff person to perform venipuncture (i.e., blood draw) as well as having the sample analyzed at a traditional laboratory. Ideally, all patients with a positive POC test should be evaluated by a clinician to assess for:

    1. signs and symptoms of primary and secondary syphilis;
    2. a sexual history to determine if this infection was acquired within the last 12 months;
    3. a neurologic assessment to ensure the patient does not have evidence of complicated syphilis infection (also known as ocular, neuro, or otic syphilis); and
    4. counseling that a positive result may reflect a false positive result, and further testing is recommended.

    If a clinician is not present, linkage to clinical care should be attempted. When possible, immediate treatment should be provided in symptomatic patients; see additional information below.

- **Neurologic symptoms:** People with a positive POC test should be screened for changes in vision, hearing, and new or different neurologic symptoms (e.g., headaches, numbness/tingling). Approximately 7% of patients with syphilis will have these symptoms and should have a further work up with the appropriate specialty provider for appropriate procedures (e.g.., ophthalmology for ocular syphilis, otolaryngology for otosyphilis, or for lumbar puncture). About half of these patients will have confirmed ocular, neuro, or otic syphilis, which when left untreated can lead to blindness, deafness, and other neurologic problems. Treatment of ocular, neuro, and otic syphilis requires a different formulation of penicillin given for 10 or more days via continuous intravenous therapy.
- **Pregnancy testing**: Pregnancy status should be assessed when appropriate for anyone with a positive syphilis POC test. People who are pregnant should be prioritized for immediate treatment, laboratory testing, follow-up, and referral for prenatal care.
- **Same day treatment**: Ideally, positive syphilis POC test results should be paired with immediate treatment with 2.4 million units of benzathine penicillin G, which requires administration by a trained health care provider. If benzathine penicillin G is not available, doxycycline 100mg twice daily for 14 days could be provided, except to those who are pregnant. Penicillin is the only acceptable treatment during pregnancy. If treatment cannot be provided at the time of the syphilis POC test result, there should be a plan in place for linkage to treatment and follow-up.

- **Determining Syphilis Stage:** Syphilis is classified as primary, secondary, latent (either early or late), or tertiary. Based on the history, physical exam, and laboratory-based test, a patient should be classified into one of these stages:

    1. Primary syphilis means the person has a lesion(s) (known as a 'chancre') at the site of infection. The chancre develops around 10 days to 3 weeks following exposure.
    2. Secondary syphilis occurs when the person has a rash or sores on mucus membranes, or other signs and symptoms of secondary syphilis. The rash can form all over the body, and often is on the palms of hands and the soles of feet. Other symptoms can include:
        - Fever
        - Swollen lymph glands
        - Sore throat
        - Patchy hair loss
        - Headaches
        - Weight loss
        - Muscle aches
        - Fatigue
    3. Latent syphilis occurs without signs or symptoms. Latent syphilis can be classified as early (the infection was acquired in the last year) or late (the infection was acquired more than 1 year ago). This difference is important to the length of treatment (see section on appropriate length of treatment).
    4. Tertiary syphilis is rare in the modern era. In this stage, the patient will have various symptoms as the infection can affect many different organ systems. Photos and additional information about syphilis staging are available at National STD Curriculum (uw.edu)

- **Appropriate length of treatment**: People with primary, secondary, or early latent syphilis, otherwise collectively known as early syphilis, can be treated with 2.4 million units of benzathine penicillin G once. However, treatment for late latent and unknown duration syphilis requires 3 weekly doses of 2.4 million units of benzathine penicillin G. To aid completion of treatment, programs need to develop a plan for the administration of the second and third shots and follow-up. If 14 days of doxycycline was provided due to the Bicillin® L-A shortage, a plan to extend the dosing by 14 days to complete the full regimen (i.e., doxycycline 100mg twice daily for 28 days) should be arranged to treat late latent and unknown duration syphilis. During pregnancy, syphilis should be treated with benzathine penicillin G.

- **Negative POC test results**: The sensitivity of POC tests is generally lower than laboratory-based tests. For best clinical care and program quality assurance, negative POC tests are followed up with laboratory-based serologic tests to help limit and evaluate false negative results.

- **Counseling, education, and outreach:** The rapid results of POC tests for syphilis create new opportunities for testing, treatment, and outreach. As with other health encounters, individuals need counseling about their sexual health; education about this test, understanding results, and the need for follow-up; and support with contacting their partners through reporting to health departments.

Which populations would benefit most from POC tests?

Since currently authorized syphilis POC tests generally have lower sensitivity and specificity than routine laboratory-based serologic syphilis tests and only provide treponemal antibody results, laboratory-based tests should be used when available. However, POC tests that provide rapid results can be useful in certain situations as listed below.

Locations with High Incidence of Syphilis Cases

POC tests should ideally be used in settings with a higher incidence of new syphilis infections to reduce the likelihood of treating individuals who may have already been treated. Settings with higher incidence can be defined in different ways, including by geographic area or a specific clinic or location with high rates of new infections.

Populations Less Likely to Have Recurrent Infections

Since POC tests detect treponemal specific antibody which can stay positive for life, they should be used in populations that are less likely to have been diagnosed and treated for syphilis in the past. **For patients with a known history of a syphilis diagnosis, serologic testing is preferred over POC tests.**

As a population, cisgender women are less likely to have recurrent infections with syphilis[9], and thus have low prevalence of previously treated syphilis. Other populations that have high incidence and low prevalence of previous diagnoses might benefit from syphilis POC tests as well. Populations and settings that may derive benefit from POC tests include:

- Persons identifying as American Indian or Alaska Native (AI/AN), particularly women (e.g., prior estimates of annualized incidence up to 2.3% in 30–34-year-old AI/AN women).[10]
- Black and Latino heterosexual persons, particularly non-Hispanic Black women who experience syphilis at rates 8-10-fold higher than non-Hispanic White women in certain parts of the country.[11]
- Persons experiencing incarceration (e.g., prior estimates of up to 1.4% prevalence of early syphilis for women in jail intake settings).[12, 13]

Effective prevention and detection of congenital syphilis relies on early routine serologic screening of pregnant people during prenatal visits. With POC tests, treatment can begin sooner.

Overcoming Barriers to Care: While the populations mentioned above have been shown to have high incidences of syphilis, it is important to remember that syphilis POC tests are primarily useful for populations that have difficulty with health care access or follow-up for test results and/or returning for treatment. Among the benefits of syphilis POC tests are that they do not require phlebotomy and that they provide rapid results. Table 2 illustrates how testing in higher prevalence populations minimizes the misdiagnoses and potential overtreatment.

Table 2: Impact of Population Prevalence on Performance of Syphilis POC Tests

	In population with true prevalence of 7.5%, if 1,000 people were tested	**In population with true prevalence of 5%, if 1,000 people tested**	**In population with true prevalence of 1%, if 1,000 people tested**
SHC Assuming sensitivity 96% and specificity 97%	72 Infections detected 3 Missed infections 28 Misdiagnosed/overtreated	48 Infections detected 2 Missed infections 29 Misdiagnosed/overtreated	9 Infections detected 1 Missed infection 30 Misdiagnosed/overtreated
Chembio DPP Assuming sensitivity 90% and specificity 96%	67 Infections detected 8 Missed infections 37 Misdiagnosed/overtreated	45 Infections detected 5 Missed infections 38 Misdiagnosed/overtreated	9 Infections detected 1 Missed infection 40 Misdiagnosed/overtreated

Which settings might consider using POC tests?

While laboratory-based serologic testing is preferred, there are some settings where POC tests with their quick results might be useful. Regardless of setting for POC tests, confirmatory serology is needed to manage care. The graph below helps summarize where lab-based serology testing is better versus POC tests.

Table 3: Choosing Lab-based Versus POC Tests

Where Lab-Based Tests Are Most Useful	**Where POC tests Are Most Useful**
Individuals with prior history of syphilis should only have lab-based tests Low risk* individual presenting for routine visit	Where identifying syphilis infection is important for same day treatment
Disadvantages of POC Tests	**Advantages of POC Tests**
Results are treponemal only and less accurate than lab-based tests If positive, lab-based tests are needed for patient care and follow-up	Results quicker than lab-based tests Easier to perform Less sample required, easier to collect
Settings for Lab-Based Tests	**Settings to Consider for POC Tests**
Where feasible and accessible Routine screening Hospital inpatient, especially if likely to stay 48 hours or more Maternal testing at delivery prior to newborn discharge (requires lab-based testing)	Correction facilities Emergency departments Substance use treatment programs Syringe service and harm reduction programs Outreach and community-based care events Rural communities Shelters
Populations Most Appropriate for Lab-Based Tests	**Populations Most Appropriate for POC Tests**
Lab-based testing should be used to confirm all positive POC tests results Low risk Populations likely to follow up if results positive Geographic areas where syphilis is not common	Pregnant people not engaged in prenatal care Persons using substances and not engaged in health care Populations with limited access to healthcare Geographic areas where syphilis is spreading rapidly

*Low risk: Based on geographic spread of disease and behavioral factors, including likelihood to follow up

Summary

Syphilis has surged over the past decade in the U.S. Many areas have increased rates and increased screening will be critical to reduce further spread.

Routine screening for syphilis should be widely adopted and laboratory-based when possible. Current authorized POC tests can generally be useful to provide rapid results and create an opportunity to identify syphilis and potentially provide same day treatment. Lower sensitivity and specificity than laboratory-based serologic testing limits syphilis POC tests' usefulness, and POC tests should not be used in those previously diagnosed with syphilis. In addition to training and quality assurance measures, additional supports are appropriate to utilize POC tests, including

- an associated laboratory that holds a CLIA certificate of waiver,
- a confirmatory serologic testing to allow for further patient care,
- the ability to provide clinical assessment and follow-up, including treatment, and
- a mechanism to report positive results to the health department, including treatment and pregnancy status (if known) and initiate partner services.

Resources

Links to Existing Algorithm and Protocols for Syphilis POC Tests:

- https://www.indiancountryecho.org/resource-hubs/syphilis-resources/
- https://www.dph.ncdhhs.gov/epidemiology/communicable-disease/syphilis-rapid-testing-algorithm/open

Additional Resources:

- CDC's Sexually Transmitted Infections (STI) Treatment Guidelines, 2021
- National STD Curriculum (uw.edu)
    - https://www.std.uw.edu/
    - https://www.nycptc.org/x/Syphilis_Monograph_2019_NYC_PTC_NYC_DOHMH.pdf

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