

“Syphilis EIAs” Frequently Asked Questions

1) What is a syphilis EIA?

A syphilis EIA is an “enzyme immunoassay.” This is a blood test for syphilis that tests for antibodies directed at the syphilis organism (*Treponema pallidum*). The EIA is a treponemal-specific test, like the TPPA or MHA-TP that have been used for many years. Syphilis CIAs (“chemoluminescence assays”) are similar to EIAs. There are a number of syphilis EIAs and CIAs available.

2) I always remember ordering an RPR when I wanted to test for syphilis. Why is my lab using a syphilis EIA or CIA?

Many commercial laboratories have adopted EIAs or CIAs for syphilis screening because they are highly automated tests, and thus are less expensive and more efficient to perform than RPRs or VDRLs. EIAs and CIAs are very sensitive and specific tests for syphilis.

3) Why is screening with an EIA instead of an RPR sometimes referred to as Reverse Sequence Syphilis Screening?

Traditionally, syphilis screening is conducted with an RPR or VDRL. Unlike EIAs, the RPR and VDRL are *non-treponemal* antibody tests. They detect antibodies to proteins that are not part of the syphilis organism itself, but are similar to proteins found in the syphilis bacteria. RPRs or VDRLs must be confirmed with a treponemal specific test; most labs use a TPPA (treponemal pallidum particle assay) to confirm a positive RPR or VDRL. Screening with a non-treponemal test and confirming with a treponemal test is sometimes referred to as “traditional sequence” syphilis screening.

Labs that screen with an EIA have “reversed” this algorithm. Rather than starting with a non-treponemal test and confirming with a treponemal test, they are starting with a treponemal test (the EIA or CIA) and confirming with a non-treponemal test (the RPR). Thus it is sometimes referred to as “reverse sequence” screening.

4) If the EIA is positive, why do I need an RPR (or VDRL)?

The RPR or VDRL provides a *quantitative* result (known as a “titer”) that is helpful for staging disease and also for establishing a baseline for determining whether the patient responds appropriately to syphilis treatment. Once the EIA is positive (i.e., the first time someone is infected with syphilis), it remains positive for life in most people, and is therefore not useful for detecting reinfection, unlike the RPR, which fluctuates with disease activity.

5) Will the EIA become negative after I treat the patient?

No, the EIA usually remains positive after treatment, but if the RPR (or VDRL) decreases fourfold after treatment, the patient has likely been cured of syphilis. Remember that individuals can get syphilis more than once, so it is important to continue screening patients who are at risk for syphilis on a regular basis (q3-6 months).

6) What does it mean if the EIA is positive and the RPR (or VDRL) is also positive?

This means the patient has current or past syphilis. You should determine the stage of disease (primary, secondary, early latent, late latent, tertiary or serofast) based on their current or recent symptoms and signs, last syphilis test results and syphilis treatment and RPR (or VDRL) titer history. If you have questions about the diagnosis or treatment of syphilis, please contact City Clinic at 415-487-5595.

7) What if the EIA is positive and the RPR (or VDRL) is negative?

This is sometimes referred to as a “discordant” result. In this situation, the CDC recommends obtaining a third syphilis test to help resolve the situation. Many labs will automatically “reflect” to a third test in this situation. Typically, this is a TPPA.

a. What if the EIA is positive, the RPR (or VDRL) is negative and the TPPA is also negative?

This is most likely a false positive EIA. No further action is necessary. If your clinical suspicion for syphilis is high, you should consider empiric treatment for syphilis, and repeat the syphilis tests in 2-4 weeks. The EIA is more sensitive for very early primary syphilis than the TPPA or RPR, so could theoretically turn positive before these other two tests.

b. What if the EIA is positive, the RPR (or VDRL) is negative and the TPPA is positive?

There are several possible explanations for these results:

1. **The patient has a history of treated syphilis.** If this is the case, no treatment is necessary. If the patient is at risk for syphilis, they should continue to be screened every 3-6 months.
2. **The patient has late latent syphilis.** In this case, the patient should be treated with Benzathine Penicillin G 2.4 mu IM weekly x 3
3. **The patient was recently exposed to syphilis and the RPR has not yet turned positive.** If your patient is at risk for syphilis, bring the patient back to clinic, do a complete oral, skin and anogenital exam to look for signs of syphilis and repeat the syphilis tests. If the patient is asymptomatic and the RPR is still negative, and the patient has never been previously treated for syphilis, they should be treated for late latent syphilis.

8) How do I know if my patient is at risk for syphilis?

- In 2019, approximately 90% of early syphilis cases in San Francisco were among men, and over 75% was among men have sex with men (MSM).
- Sexually active MSM are at risk for syphilis and should be screened regularly (q3-6 mo). Syphilis is also increasing among women in San Francisco, particularly among women experiencing homelessness, or who use stimulants.
- Syphilis in women increased by 155% between 2017 and 2019, and congenital syphilis is also increasing.
- Pregnant women should be screened for syphilis in the 1st and 3rd trimester, and again at delivery if at increased risk for syphilis.
- Non-pregnant women should be screened for syphilis at least annually if they report any of the following: Sex with a man who has sex with men, history of STD in the past year, methamphetamine use, unstable housing or homelessness, sex work, intimate partner violence, or incarceration.

Citywide STI screening guidelines are available on the SFCC website:

https://www.sfcityclinic.org/sites/default/files/2019-07/ScreeningandSurveillance_CitywideSTDscreeningguidance_0619.pdf

Reverse Sequence Screening Algorithm

	Syphilis Health Check*	EIA	RPR	TPPA	Interpretation
Turnaround	15 minutes	1 hour	Daily	Weekly (Wed)	
Description	Treponemal Test	Treponemal Test	Non-Treponemal Test	Treponemal Test	
Test Type	POCT	Lab	Lab	Lab	
Possible Results	Positive Negative	Positive Negative	Reactive with Titer Non-Reactive	Positive Negative	
Scenarios	Negative				<ul style="list-style-type: none"> Not syphilis Send lab-based test if high clinical suspicion
	Positive	Neg	No Reflex		<ul style="list-style-type: none"> Not syphilis (false positive)
	Positive	Positive	Non-Reactive	Negative	<ul style="list-style-type: none"> Repeat test in 2-4 weeks Consider empiric treatment if high suspicion or at high-risk of loss to follow-up
	Positive	Positive	Reactive	No Reflex	<ul style="list-style-type: none"> Past or present syphilis Treat based on titers, history, and physical exam
	Positive	Positive	Non-Reactive	Positive	Possible interpretations: <ol style="list-style-type: none"> Untreated early syphilis (symptoms or known exposure within 1 year) Untreated late latent syphilis (no symptoms, no known exposure) Previous syphilis treatment (follow titers)

*Syphilis Health Check (rapid test) only for patients without history of syphilis