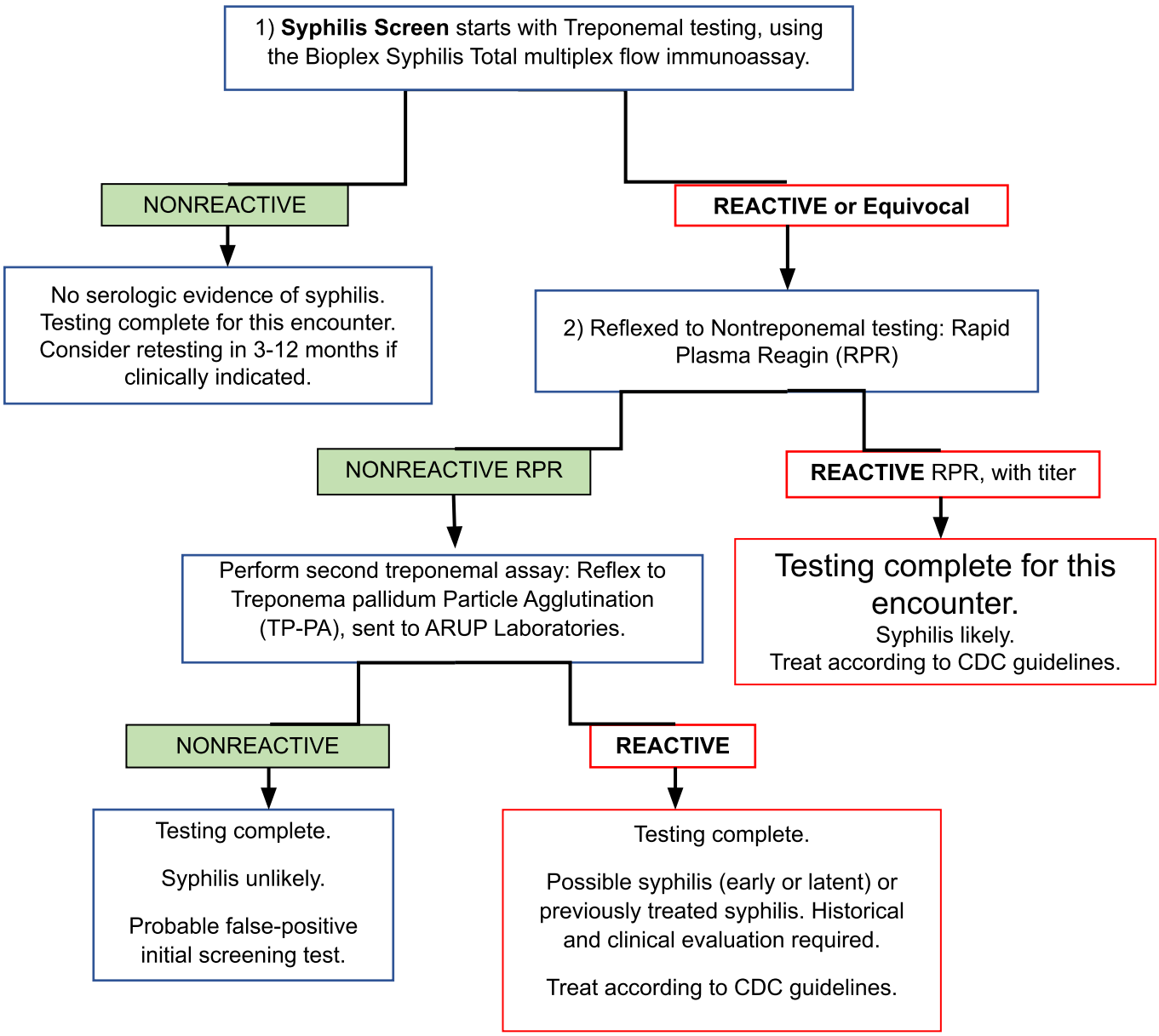
Syphilis Testing Algorithm (CHI NE/IA)

Indications for Testing:
- Persons with signs or symptoms of syphilis infection
- Asymptomatic persons at high risk for syphilis (or of transmitting the disease to others)

Testing Algorithm:



Special Neonatal testing and Treatment Monitoring:

- **Neonatal testing for congenital syphilis - order Lab315150,** RPR Neonatal Only
- **Diagnosed syphilis-positive cases undergoing treatment: order Lab315151,** RPR Treatment Monitoring Only

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Reverse Sequence Screening Algorithm Explained:

As an alternative to the traditional syphilis screening algorithm, many laboratories utilize the reverse syphilis screening algorithm. This algorithm starts with an automated treponemal assay, such as an enzyme immunoassay and multiplex flow immunoassay (MFI), to detect antibodies specific to T pallidum. If the screening assay is positive, the sample is reflexed to a RPR assay, which, if positive, is reported with a titer and is indicative of active or recent syphilis infection. If the RPR is negative, the sample is reflexed to a second treponemal assay, such as the T pallidum particle agglutination (TP-PA) assay. If the TP-PA is positive, this would indicate previously treated or late-stage syphilis infection. Alternatively, if the TP-PA is negative, the initial positive screen is interpreted as a false positive result.

Syphilis screening at CHI Health Laboratory is performed by using the reverse algorithm, which first tests sera for T pallidum specific IgG/IgM antibodies using an automated MFI. A positive treponemal test suggests infection with T pallidum but does not distinguish between recent, past, treated or untreated infections. This is because treponemal tests may remain reactive for life, even following adequate therapy. Therefore, the results of a nontreponemal assay, such as RPR, are needed to provide information on a patient's disease state and history of therapy.(Table)

In some patients, the results of the treponemal screening test and RPR may be discordant (eg, syphilis IgG/IgM positive and RPR negative). To discriminate between a falsely reactive screening result and past syphilis, a second treponemal-specific antibody test is recommended using a method that is different from the initial screen test (eg, TP-PA).

Guide to Syphilis Reverse Screening Interpretation

1) Result of 1st treponemal test **Syphilis Screen** (multiplex flow immunoassay)	2) Result of Non-treponemal **RPR** (Rapid Plasma Reagin)	3) Result of 2nd treponemal test **TP-PA** (Treponema Pallidum by Particle Agglutination)	**Interpretation**
Nonreactive	n/a	n/a	No serological evidence of infection. No further testing required, unless clinically indicated. Early or incubating syphilis infection cannot be excluded.
Reactive or Equivocal	Reactive	n/a	Presumptive evidence of infection. Likely untreated or recently treated syphilis. Follow CDC treatment guidelines.
Reactive or Equivocal	nonreactive	Reactive	Possible syphilis (eg, early or latent), *or* past, successfully treated syphilis. Thorough historical and clinical evaluation required.
Reactive or Equivocal	nonreactive	nonreactive	Likely false-positive screening test. No further testing required, unless clinically indicated.

Limitations:

- Test results should be considered with other laboratory results, as well as the clinical presentation of the patient.
- A Nonreactive Syphilis Screen test does not exclude the possibility of exposure to or infection with *T. pallidum*. Antibodies may be low or undetectable levels in incubating or early primary disease and in some clinical conditions. Therefore results must be interpreted with caution.
- Detections of treponemal antibodies may indicate recent, past or successfully treated syphilis infections are therefore cannot be used to differentiate between active and cured cases.
- Circulating antibodies against yaws, pinta and bejel may interfere with syphilis screen assay (Bioplex Syphilis Total MFI).

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NOTE: There are some situations where the full syphilis testing algorithm is not necessary or appropriate.

- Case 1: Individuals who have been confirmed by the reverse algorithm and are undergoing treatment may need RPR titers to monitor treatment progression.
- Case 2: Possible case of congenital syphilis (CS), which is a disease that occurs when a mother with syphilis passes the infection on to her baby during pregnancy. Conducting a treponemal test (e.g., TP-PA, immunoassay-EIA, CIA, or microbead immunoassay) on neonatal serum is not recommended, as results could be attributed to passively transferred maternal antibodies, which can persist for >15 months. Commercially available IgM tests are not recommended. A presumptive case of congenital syphilis occurs when quantitative nontreponemal serological titres are fourfold higher than the mother's (both drawn at birth).

CDC guidelines available at https://www.cdc.gov/std/treatment-guidelines/syphilis.htm

References:

1. Arnold, S. R., & Ford-Jones, E. L. (2000). Congenital syphilis: A guide to diagnosis and management. *Paediatrics & Child Health, 5*(8), 463–469. https://10.1093/pch/5.8.463
2. *Congenital Syphilis - STI Treatment Guidelines* (2022, -10-19). Retrieved Jul 22, 2025, from https://www.cdc.gov/std/treatment-guidelines/congenital-syphilis.htm
3. Slev, P. (2024). *Treponema pallidum - Syphilis | Choose the Right Test.* Retrieved Jul 22, 2025, from https://arupconsult.com/content/treponema-pallidum