HEALTH ADVISORY

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COVID-19 Serology Testing Guidance

BACKGROUND The novel coronavirus disease (COVID-19) pandemic has prompted the urgent need for high performing molecular (PCR) and serological tests for COVID-19. With molecular pathogen detection more readily available, there has been great interest and shift towards serological screening to determine prior exposure to SARS-CoV-2 infection. These serology assays measure antibodies against SARS-CoV-2. Due to the unique nature of this pandemic response and a goal of ramping up COVID-19 testing capacity rapidly in the United States the Food and Drug Administration (FDA) has approved many COVID-19 tests without fully understanding performance characteristics. Not all tests are created equally and some tests provide more reliable data than others. The intent of this alert is to provide general guidance for providers on COVID-19 serological assays. Please understand that this area is changing very rapidly and providers will be responsible for new changes as more serological options become available.

The PCR test is for diagnostic purposes during acute infection, while the serology test assesses for past exposure. Both tests together can provide supplementary information this is useful from a population health perspective, and are critical in implementing a comprehensive COVID-19 strategy.

Currently, serology is best used as a tool for helping us understand how the virus may be moving within a population such as a county or state and is not yet very useful for individuals to manage their health.

GENERAL CONSIDERATIONS

Serological Response

- Antibodies are usually detected 10-14 days *after* a person has had an infection. For some people it can take up to 3 weeks for antibodies to show up.
- Because COVID-19 is a new virus, we have not yet determined if the presence of antibodies in a person's system means the person is now immune to COVID-19 and if so, how long that immunity may last.
- Many serological tests measure IgG antibody response. Testing for IgG antibodies during acute symptoms, or within 14 days of symptom onset, is **not recommended**.

Serological Testing Options and Guidance

- Rapid Serology Tests
  - Due to the FDAs relaxed regulatory oversight, the market has been flooded with commercially available so called "rapid serology tests" that resemble home pregnancy tests. The technology is a lateral flow immunoassay performed on a finger-stick blood sample. They are of uncertain reliability and **not recommended** for individual use since the results – whether positive or negative – are inconclusive.
  - At this time, since the FDA did not require Emergency Use Authorization, many of these disposable tests have not been fully validated and the performance characteristics are not well established.
- Enzyme Linked Immunosorbent assays (ELISA) or automated chemiluminescent immunoassays
  - These serological assays are often run on large instruments in high-complexity clinical laboratories.

- These assays are more reliable than rapid serological tests described above.

- <u>Considerations when choosing a serological test?</u>
  - Is the serology assay FDA approved?
    - Review the serology FAQs on the FDA website – link provided below.
  - The screening performance of these tests in predicting disease (positive and negative predictive values) will vary depending on the population tested.
    - For example, at a nursing home in Washington state where 30.3% of the people tested positive for COVID-19 by PCR, the PPV of a serology test with 90% sensitivity and 97% specificity will be high (93%).
    - In contrast, if there is a 3% prevalence rate as seen in some occupational health settings, the PPV of a serology test with 90% sensitivity and 97% specificity will be low (47%).
    - For Humboldt County where the true prevalence is likely well below the referenced 3%, the test will perform even more poorly. As such, Public Health recommends targeted testing in clinical scenarios that sufficiently raise the pretest probability to an acceptable level.
  - The prevalence of disease influences the positive predictive value (PPV) for predicting antibody production following COVID-19 exposure.

Table 1: Positive Predictive Value Comparison based on Test Characteristics.

	Sensitivity 90% Specificity 97%	Sensitivity 90% Specificity 98%
Prevalence	PPV	PPV
1%	23%	31%
3.5%	52%	62%
5%	61%	70%
6%	66%	74%
7%	69%	77%
8%	72%	79%
9%	75%	82%
10%	77%	83%

Test acceptability criteria of Sensitivity and Specificity of 90% and 97% will provide 77% PPV at a COVID-19 prevalence of 10%

Serology Interpretation

- COVID-19 serological results are reportable to California Department of Public Health.
- Serological testing is not a diagnostic test for active COVID-19 infection.
- It is critically important to know:
  - A positive result does not indicate protection from future COVID-19 infections and does not definitively indicate prior exposure to COVID-19.
    - A positive IgG means you have developed an immune response to the COVID-19 virus.

        - It is unclear if a person could still spread infection to others, even if they have antibodies.
    - A negative result does not exclude either current or prior COVID-19 infection.
        - It usually takes 2 weeks to develop IgG antibodies after the start of an illness, sometimes longer. Some people may never develop antibodies if they had an infection.

Resources

US FDA – FAQs on Diagnostic Testing for SARS-CoV-2

https://www.fda.gov/medical-devices/emergency-situations-medical-devices/faqs-diagnostic-testing-sars-cov-2

California COVID-19 Testing Task Force, Testing Options Work Group – Serology Testing Public Guidance

https://testing.covid19.ca.gov/wp-content/uploads/sites/332/2020/04/Serology-Testing-Public-Guidance.pdf

Infectious Diseases Society of America (IDSA) – COVID-19 Antibody Testing Primer

https://www.idsociety.org/globalassets/idsa/public-health/covid-19/idsa-covid-19-antibody-testing-primer.pdf

Thank you for your hard work and cooperation during this pandemic response.