PDL UPDATE: PDL Serology Testing Update

April 20, 2020

Pacific Diagnostic Laboratories (PDL), in addition to the antigen testing PDL has made available, is actively researching and developing a strategy for antibody (serology) testing for COVID-19. The landscape for this testing is very dynamic with the medical community's understanding of antibody (Ab) testing progressing every day. Many vendors are submitting for Emergency Use Authorization (EUA). PDL has chosen to implement Diazyme's platform for Ab testing that has been submitted to the FDA for EUA approval.

Overview of Antibody Testing and Capabilities:

- Ab testing could indicate whether someone is immune to SARS-CoV-2. This testing could delineate immune individuals from those who remain susceptible. The effectiveness of Ab testing hinges on whether everyone who has contracted SARS-CoV-2 actually develops antibodies, whether those antibodies protect against secondary infections, and if so, how long the antibodies stay in the body and remain protective. Ab testing does not indicate whether the patient is currently infected; therefore, a negative result does not rule out whether a patient is contagious. Ab test results can also be useful for widespread disease surveillance and epidemiological research.
- Ab titers can help identify individuals who may qualify to donate blood that can be used to manufacture convalescent plasma, an investigational product that may be useful treating patients infected with COVID-19.

PDL's Current Ab Strategy:

1. Acquisition of Diazyme L-300 immunoassay IgG/IgM on serum or plasma (capacity 500-1000/day).
2. Establish a dual testing strategy with Ag and Ab testing to optimize clinical sensitivity.
3. Assess the use of a single platform solution that tests for both Ag and Ab.
    a. Core lab – high volume throughput on current immunoassay platform.
    b. POC – multipurpose platform that is capable of running highly sensitive Ag/Ab methods.
4. Depending on hospital and community demand, implement an EUA approved lateral flow Ab assay to start testing as soon as possible.

FDA EUA Approved Antibody Tests (as of 4/20):

- **Cellex:** Lateral flow-manual (LFM) using venipuncture whole blood
- **Chembio:** Lateral flow-optical (LFO) using fingerstick or venipuncture whole blood
- **Ortho Clinical (OCD):** Vitros automated immunoassay analyzer using serum or EDTA plasma

Risks and Considerations:

1. **Availability of supplies:**
   Whereas many laboratories do not have MDx platforms to leverage, most labs have high throughput immunoassay analyzers, often coupled with chemistry analyzers on a track-based system. Vendors selling automated chemistry/Immunoassay platforms have indicated their intent to commercialize Ab assays.
2. **Approved Use — IFUs and off-label use:**
    a. EUA approved Ab test kits are designated H (high complexity), M (moderate complexity) or W (Waived) at the time of approval and listed on the FDA website. To date, all 3 EUA approved Ab kits are designated H, M.
    b. All 'off-label' use of an EUA approved kit or all 'registered' Ab test kits not EUA approved are considered LDTs (lab developed tests) by the FDA and CLIA and as such carry an H designation and must be performed in a high complexity approved laboratory. Even if the method is a lateral flow immunoassay (with or without optical reader), and the IFU indicates fingerstick whole blood as an acceptable specimen type, all LDTs must be performed in a high complexity lab, and cannot be performed under a waived setting unless specifically designated in the IFU and EUA approval letter.

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3. Accuracy

Absent an FDA template defining validation requirements, Ab assays do not carry standardized performance specifications, yet most claim sensitivities and specificities above 90%. Unfortunately, a key indicator of performance identifying the # of days blood is drawn post symptoms is often not included in the Instructions for Use (IFU). The longer the window between symptoms and blood collection increases the likelihood of Ab presence, so higher claims of sensitivity may be more reflective of the timing of testing than the actual analytical performance. There have been numerous reports in the literature indicating that the actual performance of several Ab kits does not meet performance claims, resulting in a high # of false negatives (and to a lesser extent) and false positives.

Frequently Asked Questions:

Q: What considerations are there for using serology tests to predict COVID-19 prevalence?

A: The screening performance of these tests in predicting disease (positive and negative predictive value) will vary depending on the prevalence of COVID-19 in the population tested. For example, at the 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%).

Q: What types of serological testing methods exist?

A: Testing methods range from simple disposable lateral flow assays (LFA) used as a point-of-care test to enzyme-linked immunosorbent assays (ELISA) or automated chemiluminescent immunoassays run on large instruments in clinical laboratories.

Q: Where can serological tests be performed?

A: At this time, most platforms are considered moderate or high complexity under the Clinical Laboratory Improvement Amendment (CLIA) and must be performed at appropriately certified labs. Point-of-care kits that receive FDA emergency use authorization and are designated waived are an exception and are considered CLIA-waived for the duration of the national emergency declaration.

Q: Are rapid disposable serology test kits (lateral flow assays) reliable?

A: Rapid disposable serology test kits are of uncertain reliability. 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. They are not recommended for individual use unless they have been approved under the FDA EUA process.

Please feel free to call our Client Service Center with any questions at 805-879-8100.

On behalf of all of us at PDL, thank you for the care you are providing. We hope this COVID-19 Ab update will help understand our efforts to provide you with the necessary information to keep appraised of the rapid developments taking place.

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