Warde Medical Laboratory

Warde Medical Laboratory COVID-19 IgG Antibody Testing

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Beginning on Tuesday May 12, 2020, Warde Medical Laboratory will offer serologic testing for IgG antibodies to SARS-CoV-2, the causative agent of the Coronavirus Disease-19 (COVID-19) infection. Analysis will be performed using a method developed and validated by DiaSorin, Inc on the Liaison XL diagnostic platform. This method has received emergency use authorization (EUA) by the US Food and Drug Administration (FDA) for use during the COVID-19 public health emergency.

Serologic testing for anti-SARS-CoV-2 antibodies has been the subject of much discussion, debate, and controversy. Although the presence of antibodies to SARS-CoV-2 indicates likely exposure to the virus, the US Centers for Disease Control and Prevention notes "We do not know yet if the antibodies that result from infection with SARS-CoV-2 can protect someone from reinfection with this virus or how long antibodies to the virus will protect someone."(1) Furthermore, while many commercially available SARS-CoV-2 antibody kits list high rates of sensitivity and specificity at the level of populations, the individual predictive value of even highly sensitive and specific tests may be relatively low in the setting of low disease prevalence. (2) As such, it may be difficult to determine on an individual basis the likelihood of previous infection in the setting of a positive serology test.

FDA has allowed a framework for serologic testing to be marketed and performed in the US under emergency use authorization in response to a public health emergency. Prior to May 4, 2020, individual manufacturers or individual laboratories were allowed to market their serologic assays without review or clearance by FDA as long as the manufacturer or laboratory had validated the assay, and as long as the manufacturer or laboratory had agreed to certain disclaimers. The disclaimers included statements that the test had not been reviewed by FDA and the potential for the assay to cross-react with antibodies to other non-SARS coronaviruses. This was the so-called "Policy IV.D" pathway, named after the section of the FDA's Policy for Diagnostic Tests for COVID-19 During the Public Health Emergency, published on-line in March, 2020.(3) However, manufacturers or individual laboratories also may submit to FDA for Emergency Use Authorization (EUA)—a higher level of authorization that does subject the method to FDA review. Effective May 4, FDA now requires all manufacturers who notified them under "Policy IV.D" to submit for EUA. The DiaSorin assay performed at Warde received EUA from FDA on April 26, 2020.(4)

In validating their assay for use, DiaSorin tested over 1,000 serum samples obtained from individuals prior to the COVID-19 outbreak for potential cross-reactivity, and claims a 99.3% clinical specificity (95% Confidence Interval: 98.6 – 99.6%). The sensitivity of the assay depends upon the time the testing is done relative to symptom onset. Based on limited sample data, DiaSorin claims a sensitivity of 97.5% (95% CI: 87.4 to 99.6%) for samples taken at least 15 days after initial diagnosis. Predictably, sensitivity is lower at shorter time intervals after initial diagnosis, since it takes time to develop antibodies. Sensitivity at =<5 days is claimed as 25%, and sensitivity at 6 to 14 days is claimed as 89.8%.(5) As noted above, however, the positive predictive value (i.e. the likelihood that an individual has been infected given a positive test result) may be low for any test in the setting of a low populational prevalence of disease, even in the setting of relatively high sensitivity and specificity. Exact predictive values for serologic assays for SARS-CoV-2 antibodies have not been determined.

Warde is choosing not to offer IgM serologic testing for SARS-CoV-2 at this time. Although there is evidence that the inclusion of IgM antibodies may increase sensitivity, it is also true that IgM antibody serology should not be used to diagnose acute or active COVID-19 disease, and in general IgM serologic testing for infectious agents likely carries with it a higher false-positive potential than does IgG serology. The appropriate test for detection of active or acute COVID-19 disease is a nucleic acid-based/ molecular assay.

The FDA requires that a fact sheet be made available for patients and healthcare providers regarding this test.

The fact sheet for patients may be found at:
http://www.wardelab.com/Diasorin_SARSCoV2_antibody_fact_sheet_for_patients.pdf

The fact sheet for healthcare providers may be found at:
http://www.wardelab.com/Diasorin_SARSCoV2_antibody_fact_sheet_for_health_care_providers.pdf.

In summary, the use of anti-SARS-CoV-2 antibody testing on a large scale is likely to be of benefit to population health and to epidemiologic study and planning. The value of a serologic result to any given individual, however, has yet to be clearly elucidated. The World Health Organization strongly cautions against the use of individual serologic status for the inference of presumed functional immunity, and warns that "…there is not enough evidence about the effectiveness of antibody-mediated immunity to guarantee the accuracy of an 'immunity passport' or 'risk-free certificate.'" (6)

The DiaSorin Liaison SARS-CoV-2 IgG antibody test may be ordered under Warde test code COV2G. Please call our client services line at 800-760-9969 for additional information.

References.

1. Centers for Disease Control and Prevention (CDC): Frequently Asked Questions. https://www.cdc.gov/coronavirus/2019-ncov/faq.html#Symptoms-&-Testing (accessed April 27, 2020).
2. Finn WG: Editorial: Pre-test probability matters—a comment regarding "shotgun" testing. Warde Report 2013; 23(1): http://www.wardelab.com/edit_23_1.html (accessed April 27, 2020).
3. US Food and Drug Administration, Center for Devices and Radiological Health: Policy for diagnostic tests for coronavirus disease-2019 during the public health emergency. Immediately in effect guidance for clinical laboratories, commercial manufacturers, and Food and Drug Administration Staff. https://www.fda.gov/media/135659/download (accessed April 27, 2020).
4. US Food and Drug Administration: https://www.fda.gov/media/137356/download (accessed April 27, 2020).
5. Diasorin, Inc: Liaison SARS-CoV-2 S1/S2 IgG, Instructions for Use. https://www.fda.gov/media/137359/download (accessed April 27, 2020).
6. World Health Organization: "Immunity passports" in the context of COVID-19: scientific brief. https://www.who.int/news-room/commentaries/detail/immunity-passports-in-the-context-of-covid-19 (accessed April 27, 2020).