FACT SHEET FOR HEALTHCARE PROVIDERS

ImmunoPass Rapid Test for COVID19 Neutralizing Antibodies

AXIM Biotechnologies/Empowered Diagnostics **September 14, 2020**

CORONAVIRUS DISEASE 2019 (COVID-19)

This Fact Sheet informs you of the significant known and potential risks and benefits of the emergency use of TRU-19 Rapid Test for COVID19 Neutralizing Antibodies (TRU-19).

TRU-19 is authorized for semi-quantitative measurement of antibodies that block the binding of SARS-CoV-2 Receptor Binding Domain (RBD) to Angiotensin Converting Enzyme 2 (ACE2) in human serum and plasma (dipotassium EDTA, lithium heparin and acid citrate dextrose (ACD)).

All individuals whose specimens are tested with the test will receive the Fact Sheet for Recipients: IMMUNOPASS RAPID TEST FOR COVID19 NEUTRALIZING ANTIBODIES.

IMMUNOPASS SEMI-QUANTITATIVELY MEASURES LEVELS OF ANTIBODIES THAT NEUTRALIZE HUMAN SARS-COV-2 AS PART OF THE HUMAN ADAPTIVE IMMUNE RESPONSE TO THE VIRUS. THE INDICATION FOR THIS TEST IS USING ONLY SERUM OR PLASMA SPECIMENS.

WHAT ARE THE SYMPTOMS OF COVID-19?

Many individuals infected with COVID-19 develop symptoms of acute respiratory illness that may include fever, chills, cough, shortness of breath or difficulty breathing, fatigue, muscle aches, headache, sore throat, runny nose, new loss of taste or smell, nausea, vomiting or diarrhea. Current knowledge about the virus that causes COVID-19, suggest that the median incubation period after infection with the virus is 5 days, but signs and symptoms may appear any time from 2 to 14 days after exposure.

Public health officials continue to identify geographic locations of COVID-19 spikes throughout the world, including regions in the United States. Travel to and from these areas increases risk of infection and affects public health. Please check the CDC webpage for the most up to date information on hotspots of infection.

WHAT DO I NEED TO KNOW ABOUT COVID-19 ANTIBODY TESTING?

Current information on COVID-19 for healthcare providers is available at CDC's webpage, Information for Healthcare Professionals (see links provided in "Where can I go for updates and more information" section)

- The ImmunoPass Neutralizing Antibody Test can be ordered by healthcare providers for testing human serum and plasma (dipotassium EDTA, lithium heparin and ACD) to measure levels of neutralizing antibodies to COVID-19, i) in units of convalescent plasma, or to monitor neutralizing antibody levels in patients during infusion, ii) to assess protection from re-infection, iii) to determine potential to transmit the virus to others and iv) to evaluate vaccine efficacy.
- ImmunoPass should not be used to diagnose or exclude acute infection. Direct testing for SARS-CoV- 2 should be performed if acute infection is suspected.
- ImmunoPass is authorized for use only in laboratories certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, to perform moderate and high complexity tests.
- Please refer to the ImmunoPass instructions for use for additional information.

REPORT ADVERSE EVENTS, including problems with test performance or results, to MedWatch by submitting the online FDA Form 3500 (**https://www.accessdata.fda.gov/scripts/medwatch/index.cfm?action=reporting.home**) or by calling **1-800-FDA-1088**

Specimens should be collected with appropriate infection control precautions. Current guidance for COVID-19 infection control precautions are available at the CDC's website (see links provided in "Where can I go for updates and more information" section).

Use appropriate personal protective equipment when collecting and handling specimens from individuals suspected of having COVID-19 as outlined in the CDC Interim Laboratory Biosafety Guidelines for Handling and Processing Specimens Associated with Coronavirus Disease 2019 (COVID-19). For additional information, refer to CDC Interim Guidelines for Collecting, Handling, and Testing Clinical Specimens from Persons Under Investigation (PUIs) for Coronavirus Disease 2019 (COVID-19) (see links provided in "Where can I go for updates and more information" section).

There are no approved available alternative tests. FDA has issued EUAs for other antibody tests that can be found at **https://www.fda.gov/emergencypreparedness-and-response/mcm-legal-regulatoryand-policy-framework/emergency-useauthorization#2019-ncov**.

WHAT DOES IT MEAN IF THE TEST INDICATES:

1. **HIGH LEVELS OF NEUTRALIZING ANTIBODIES?**

   Neutralizing antibodies prevent SARS-CoV-2 from infecting cells. In the setting of COVID19 convalescent plasma (CCP), high levels of neutralizing antibodies correlate with neutralization titers higher than 1:320 in a pseudotype SARS-CoV-2 virus assay. Infusion of CCP with high levels of neutralizing antibodies is thought to improve clinical outcome by preventing subsequent infection of host cells. High levels of neutralizing antibodies in CCP also suggest a lower dose of CCP might be infused (e.g. one unit instead of two). The sensitivity of the test indicating high levels of neutralizing antibodies is 96.8% with a positive predictive value of 81.1%.

2. **MODERATE LEVELS OF NEUTRALIZING ANTIBODIES?**

   Neutralizing antibodies prevent SARS-CoV-2 from Moderate levels of neutralizing antibodies correlate with neutralization titers between 1:320 and 1:80 in viral pseudotype assays. Infusion of CCP containing moderate levels of neutralizing antibodies should be performed with caution, as it would not be expected to provide the same clinical benefit as CCP with high levels of neutralizing antibodies despite being derived from an individual who has recovered from COVID19.

3. **LOW/NO LEVELS OF NEUTRALIZING ANTIBODIES?**

   Low or no levels of neutralizing antibodies correlate with low titers (≤1:80) in pseudotype virus neutralization assays. Infusion of CCP with low or no neutralizing antibodies would not be expected to provide significant clinical benefit. The negative predictive value of this test is 99.1%.

A false positive test result of high levels of neutralizing antibodies could be obtained if the sample has elevated levels of blood proteins that prevent the interaction of RBD with ACE2. Some children (6 mo – 17 yrs) have been shown to have elevated levels of ACE2 (13-100U/ml) compared to adults (9-67U/ml). However, since children rarely donate plasma this is unlikely to occur. A false negative test result my occur when a sample neutralizes COVID19 when the test indicates that it does not. There may be other mechanisms of neutralizing SARS-CoV-2 including antibodies to the N-terminal domain of spike protein that are not measured by this test. It is not known if or why neutralizing antibodies might be generated to non-RBD regions of spike exclusively that would not be measured by this test.

Laboratory test results should always be considered in the context of clinical observations and epidemiological data in making patient management decisions.

All laboratories using this test must follow the standard confirmatory testing and reporting guidelines according to their appropriate public health authorities.

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WHAT IS AN EUA?

The United States FDA has made this test available under an emency access mechanism called an Emergency Use Authorization (EUA). The EUA is supported by the Secretary of Health and Human Service's (HHS's) declaration that circumstances exist to justify the emergency use of in vitro diagnostics (IVDs) for the detection and/or diagnosis of the virus that causes COVID-19.

An IVD made available under an EUA has not undergone the same type of review as an FDA-approved or cleared IVD. FDA may issue an EUA when certain criteria are met, which includes that there are no adequate, approved, available alternatives, and based on the totality of scientific evidence available, it is reasonable to believe that this IVD may be effective in the detection of the virus that causes COVID-19.

The EUA for this test is in effect for the duration of the COVID-19 declaration justifying emergency use of IVDs, unless terminated or revoked (after which the test may no longer be used).

WHERE CAN I GO FOR UPDATES AND MORE INFORMATION?

CDC webpages:

General: https://www.cdc.gov/COVID19

Healthcare Professionals: https://www.cdc.gov/coronavirus/2019-nCoV/guidance-hcp.html

Information for Laboratories: https://www.cdc.gov/coronavirus/2019-nCoV/guidance-hcp.html

Laboratory Biosafety: https://www.cdc.gov/coronavirus/2019-nCoV/lab-biosafety-guidelines.html

Isolation Precautions in Healthcare Settings: https://www.cdc.gov/coronavirus/2019-ncov/infection-control/control-recommendations.html

Specimen Collection: https://www.cdc.gov/coronavirus/2019-nCoV/guidelines-clinical-specimens.html

Infection Control: https://www.cdc.gov/coronavirus/2019-ncov/infection-control/index.html

FDA webpages:

General: www.fda.gov/novelcoronavirus

EUAs: (includes links to recipient fact sheet and manufacturer's instructions) https://www.fda.gov/medical-devices/emergency-situations-medical-devices/emergency-use-authorizations-medical-devices

Contact Information:

Name: Empowered Diagnostics, LLC.

Address: 3341 West McNab Road

Pompano Beach, FL 33069

Contact telephone: +1 (954) 354-2768

Technical: info@empdx.net

Name: Axim Biotechnologies. Inc

Address: 6191 Cornerstone Court East, Ste. 114

San Diego, CA 92121

Contact telephone: : +1 (858) 405-1266

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