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April 5th, 2020

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RE: Guangzhou Wondfo Biotech Co., Ltd. SARS-CoV-2 Antibody Test and MDBox for Hays County residents

Dear Commissioner's Court:

Thank you for the opportunity to provide input on the use of antibody testing in Hays County in response to the SARS-CoV-2 (COVID-19) pandemic. As we understand, the intent of increasing antibody test kits in partnership with the telemedicine provider group MDBox in Hays County is: 1) to overcome reported shortages of testing capabilities in Hays County, 2) to provide access to drive-through testing sites in Hays County in consultation with a telemedicine provider group, MD Box, and 3) to maintain and monitor ongoing data about the prevalence of COVID-19 in Hays County.

Please see our joint response below based on our review of the current medical literature regarding COVID-19, Centers for Disease Control guidelines on COVID-19, and phone

conversations with Dr. Henry J. Legere III, MD, Chief Executive Officer for Reliant Immune Diagnostics on April 2nd, 2020 and April 4th, 2020 as well as discussions with representatives from the Hays County Health Department.

Our consensus regarding this proposal is summarized at the conclusion of this letter.

Background

Due to a history of testing shortages and long turn-around times during the early stages of the COVID-19 pandemic, a number of COVID-19 testing kits have been created to expedite and expand testing capabilities.

Currently, the Centers for Disease Control (CDC) has stratified recommended criteria for testing into four priority areas outlined below:

- **Priority 1**
    - Hospitalized patients who have signs and symptoms compatible with COVID-19
    - Symptomatic health care workers
- **Priority 2**
    - Patient in long-term care facilities with symptoms
    - Patients under 65 years of age and older with symptoms
    - Patients with underlying conditions with symptoms
    - First responders with symptoms
- **Priority 3**
    - As resources allow, test individuals in the surrounding vicinity of hospitals experiencing an increasing number of cases to decrease community spread, and ensure health of essential workers
        - Critical infrastructure workers with symptoms
        - Individuals who do not meet any of the above categories with symptoms
        - Health care workers and first responders
        - Individuals with mild symptoms in communities experiencing high COVID-19 hospitalizations
- **NON - Priority**
    - Individuals without symptoms

It is important to understand the concepts of illness, infectivity, and immune response. Illness is the presence of symptoms or "sickness" in association with exposure to a certain pathogen or disease. Infectivity is the ability to pass a certain pathogen to another individual. Immune response is the reaction of the body to a certain pathogen or disease.

Currently, there are two categories of tests being used for COVID-19.

RT-PCR method

Tests that have been given FDA approval are based on the technique of RT-PCR that detects SARS-CoV-2 specific proteins in patient secretions obtained via throat and nasal swabs. It is important to note that the presence of viral proteins in a patient's secretions does not necessarily indicate the presence of illness but does indicate a person's *infectivity*. Recent reports indicate an estimated 20% of individuals exposed to COVID-19 are thought to be asymptomatic shedders.

Molecular tests based on patient secretions (e.g. RT-PCR) are the only tests that directly assess for the presence of viral proteins in secretions. If used broadly across a population, these tests assess the prevalence of viral shedding within a community, and thus the risk of exposure from person-to-person spread of the virus via respiratory droplets.

In the future, expansion of RT-PCR/molecular testing to a larger population within the community (including asymptomatic individuals) has the potential to guide decisions regarding the ongoing need for social distancing and other initiatives that were implemented to decrease person-to-person spread. However, testing would need to be broad and such efforts are not yet in line with current CDC recommendations, as this would necessarily include Non-Priority populations as described above.

Immunoglobulin method

Recently, in contrast to FDA-approved molecular tests that detect the presence of virus in a person's secretions, serology tests have been developed for use in the COVID-19 pandemic. Serology tests detect the presence of a specific immune response (serum antibodies to COVID-19) in a blood sample. While there are a number of these testing products now on the market, the Guangzhou Wondfo Biotech Co., Ltd. SARS-CoV-2 Antibody Test is one example.

(*Note recent exception to FDA approval status: On April 3rd, 2020, the FDA granted the first emergency authorization for rapid antibody blood test for COVID-19, developed by Cellex. Its use is restricted in that it must not be used as the sole method for testing a patient with COVID-19.)*

Serology tests work by detecting the development of antibodies (i.e. immune response) to Coronavirus infection. While these tests carry relatively high specificity (accuracy in detecting absence of disease) for COVID-19, its sensitivity (accuracy in detecting presence of disease) is not nearly as high. A number of factors contribute to this discrepancy.

First, there is a small degree (10-15%) of cross-reactivity with an immune response to the more common types of Coronaviruses (HKU1, NL63, 229E, OC43) that cause the common cold. Patients who are infected or have recently been infected by other viruses that are similar to COVID-19 may trigger a false positive test result. In some individuals with other diseases (e.g. autoimmune diseases), the immune response is similar enough to create a positive result on

the serology test. It is critical to note that these tests do not directly detect COVID-19 viral proteins but rather the presence of an immune response to the infection.

Second, the average person takes 7-10 days after onset of illness to mount an immune response. Therefore, serology tests performed within the first 5-7 days of illness will not successfully detect an immune response. This limits the utility of serology test to guide early treatment and/or isolation decisions. Because of the lag time between onset of illness and detection of an immune response, repeat testing is encouraged in 5-7days if the initial serology test is negative and an individual has persistent symptoms (fever, cough, shortness of breath, or sore throat).

Historically, serology tests have been used in healthcare settings to evaluate prior exposure to a particular infection. When used in a single patient, serology tests can assess risk of developing an illness (e.g. arthritis after exposure to Lyme disease); when used more broadly across a population, serology tests can detect the development of herd immunity as more of the population acquires an immune response (similar to vaccine driven immune response). Herd immunity is the resistance to the spread of a contagious disease within a population due to the presence of a sufficiently high proportion of individuals with known immunity to the disease. However, serology tests do not detect the presence of illness nor infectivity and, therefore, are *not* used for acute management of an illness. Additionally, serology tests cannot be used as a marker for ongoing infectivity with a community.

To date, it is not known whether individuals with an immune response to COVD-19 continue to shed virus. Only molecular (RT-PCR) tests can detect whether a patient has an ongoing viral load and is therefore shedding the virus in respiratory droplets. For the sake of an individual seeking to assess his or her risk of becoming critically ill with COVID-19, neither RT-PCR nor serologic tests can predict whether or not a person will develop illness nor the degree of severity. For this reason, only those individuals that were ill enough to require hospitalization and healthcare workers treating them, received the highest priority for initial molecular testing.

The bullet points below summarize how the results of a serology test for COVID-19 should be interpreted:

- Negative test result:
    - Either a person has not been exposed to COVID-19; or
    - Testing was conducted too early in the course of illness to determine whether or not an immune response had formed. (**false negative**)

- Positive test result:
    - Indicates prior exposure to COVID-19 (or similar virus) with subsequent development of an immune response. Yet, the current illness may or may not be due to COVID-19; or

- A **false positive** test result (immune response to something other than COVID-19) which is of greater risk in individuals with auto-immune disease and/or recent infection with a number of other viruses including those that cause common colds, influenza, and mononucleosis.

Should a patient misunderstand the potential for a false negative result, re-integration into community or family activities carries the risk of infecting other individuals. Thus, patients who are lost to follow up carry high risk of further spreading the infection within the community. To reiterate, regardless of the serology test result, the presence of viral shedding (i.e. infectivity) would be unknown. Because a negative test result neither confirms the absence of infection nor lessens the need for confirmatory testing, the utility of serology testing is limited for a symptomatic patient and potentially prolongs the time to diagnosis. For others, false positive test results could result in unnecessary, prolonged quarantine in the absence of confirmatory molecular testing.

MDBox/Valiant/Antibody test

Per the Hays County MD Box COVID Task Force pamphlet, symptomatic patients would undergo screening criteria for serology testing via consultation with a physician. The screening criteria for the Guangzhou Wondfo Biotech Co., Ltd. SARS-CoV-2 Antibody Test align with the priority groups outlined by the CDC. Thus, only symptomatic patients who screen positive would undergo further testing (~1-2 % of symptomatic individuals screened). This limits the ability of this test to monitor and establish the prevalence of immunity within Hays County. As mentioned previously, when serology testing is used more broadly within a community (regardless of presence or absence of symptoms), the prevalence of exposure and subsequent development of herd immunity can be predicted. In this manner, it might be used to determine when a community has reached a high state of immunity to the disease. However, when used only on a subpopulation within the community (e.g. symptomatic individuals), an antibody test alone cannot detect the prevalence of infection nor viral shedding in the community.

(Note: On March 28th, 2020, San Miguel County in Colorado announced the use of antibody testing on all 8,000 residents to assess presence of exposure and immunity to COVID-19 using an antibody test developed by United Biomedical/COVAXX.)

Testing Availability in Hays County

The Hays County Health Department is currently reporting no shortages of RT-PCR testing for the priority groups listed above. Although resources were initially in short supply, multiple testing sites have since opened, serving both the general public and health care personnel. The health department is able to confirm that these testing sites are operational and available to the public without reported shortages of any kind.

In conclusion:

1) Hays County currently maintains sufficient numbers of FDA-approved molecular tests and testing sites within Hays County to support priority testing groups per CDC guidance.
2) Serology test results carry a high risk of being misinterpreted by both patients, healthcare workers, and the community. Great care would be need to ensure that negative results are not used to clear individuals back to work or normal activities within the community and would require partnership with the Hays County Health Department to ensure patients are: 1) not lost to follow up, and 2) receive confirmatory RT-PCR testing.
3) Serology tests may prolong time to diagnosis and cause unnecessary quarantine for certain individuals.
4) Serology testing is unlikely to reduce the need for RT-PCR testing, and may lead to increased need for FDA-approved molecular testing to confirm serology test results.
5) Use of the Guangzhou Wondfo Biotech Co., Ltd. SARS-CoV-2 Antibody Test in the manner described by the manufacturer will not reliably monitor or track prevalence of COVID-19 immunity in Hays County as only a small percentage of residents would receive testing.
6) The Guangzhou Wondfo Biotech Co., Ltd. SARS-CoV-2 Antibody Test and MD Box platform in Hays County does not fill a critical gap in the current Hays County COVID response.

Thank you,

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