From: "Pescatore, Richard (DHSS)" <Richard.Pescatore@delaware.gov>
Date: April 13, 2020 at 4:39:56 PM CDT
To: Charlie Balentine <cbalentine@pblabs.com>
Subject: Re: FAQ

Hi Charlie---this is OK for sharing

To-date, Delaware has had a good experience with the rapid lateral flow immunoassays, with some important lessons learned. Operationally, that includes the importance of an adequate blood sample (truly "super-saturating" the well), only implementing with appropriate pre-test probability, and ensuring a knowledgeable clinician is on hand to interpret the test results within the clinical scenario.

There is little doubt at this point that the tests have a significant role to play as part of a broader test strategy. We have seen limitations in our ability to mobilize other testing strategies, including PCR and rapid antigen testing, due to various chokepoints including shortages in collection materials, viral extraction reagents, platform-specific reaction reagents, capacity, and more. Following receipt of the first shipment of rapid lateral flow immunoassays ("rapid tests"), we performed validation with both known positive and known negative samples. We synthesized these data with information shared from partners in South Florida, as well as the MGH and NYU experiences. Thus far, more than 100 known SARS-CoV-2 naïve samples, including a number of samples *known* to contain antibodies to non-SARS-CoV-2 coronaviridae, have not produced a single false positive IgG . Certainly, we have gained confidence in the specificity of these assays.

The sensitivity of the tests is, of course, a consideration. In symptomatic patients, we assume many will not mount an IgM response until 2-3 days after symptoms start, and note recent publications suggesting low- or absent immune response in some patients, as well as an inverted IgG/IgM timeline of response in some patients. Nonetheless, we have been able to devise testing schema that harnesses the tests' powers of specificity while limiting any impact of lack of sensitivity. Specifically, we feel confident that the use of rapid tests in the asymptomatic population and identification of an IgG absent an IgM, is enough to consider the patient to have had remote and recovered exposure to COVID-19, and to have mounted some measure of serological immunity. Furthermore, we consider a positive IgM or IgG (or both) in a symptomatic patient to be a true positive for COVID-19 infection, thus sparing the need for PCR, which may be profoundly difficult to obtain, especially in vulnerable populations in whom there is no mechanism of effective follow-up.

We have already employed these tests in outbreak investigations, again harnessing the specificity but also leveraging a Bayesian interpretation of simultaneous testing of congregate populations. By doing so, we have been able to identify COVID-19 outbreaks in high-risk congregate settings in minutes. A "safety net" of PCR is sent on all Ig-negative patients, thus preventing any true "downside" of these tests. In

fact, we have found that the very process of rapid testing helps underscore and reinforce the importance of isolation of symptomatic persons---a fundamentally obvious maneuver, but one that we have found was not being followed in some scenarios due to the confusion surrounding COVID-19.

We have partnered with private, community, and other governmental stakeholders to develop guidelines for implementation as well as instructions for test interpretation to help safely implement wide distribution. Importantly, I feel that these tests help "get more doctors in the fight," i.e. giving community partners and potentially, primary care offices,a mechanism of contributing to a broad testing effort.

Finally, it seems likely that the identification of IgG absent IgM is sufficient to proceed to the next phase of donation for convalescent plasma.

To be clear, we have not yet "perfected" our algorithm for broad dissemination, but after multiple revisions, tabletop scenarios, and extensive discussions among a dedicated and knowledgeable multidisciplinary team of physicians, scientists, and emergency operations and disaster management professionals, we are confident in future implementation.

Richard Pescatore, DO, FAAEM
Chief Physician
Delaware Department of Health and Social Services
Division of Public Health
Jesse S. Cooper Building
417 Federal Street, Dover, DE 19901
856-305-3863
richard.pescatore@delaware.gov