June 15, 2020

American Clinical Laboratory Association

Robert Redfield, M.D.
Director
U.S. Centers for Disease Control and Prevention
1600 Clifton Road
Atlanta, GA 30333

Dear Dr. Redfield:

I am writing in response to CDC's May 27 guidance, "Interim Guidelines for COVID-19 Antibody Testing." While ACLA appreciates the CDC's continuing pandemic response efforts and efforts to educate the public on the appropriate use of antibody tests and the importance of accurate and reliable testing, we are concerned that the May 27 guidance could have the unintended consequence of limiting access to necessary COVID-19 testing (specifically antibody testing). We respectfully urge the CDC to update the May 27 guidance expeditiously to reflect current scientific evidence and to clarify the appropriate use of antibody testing as one factor, among several, in reopening decisions.

As you know, a dozen ACLA member laboratories have taken unprecedented steps to expand capacity for COVID-19 testing in the United States and have performed over eleven million COVID-19 PCR tests and millions of serology antibody tests since the beginning of March. To date, SARS-CoV-2 molecular tests have been the primary mechanism to detect the presence of viral RNA. The introduction of antibody testing — also known as serology — provides a valuable tool to assess an individual's exposure history and inform a better understanding of the timing and spread of the virus. Both PCR tests and serologic tests contribute to SARS-Cov-2 prevention, containment and mitigation strategies.

CDC's May 27 guidance, "Interim Guidelines for COVID-19 Antibody Testing" provides recommendations on the use of serologic tests in clinical and public health settings. First and foremost, ACLA appreciates CDC's efforts to educate the public on the appropriate use of antibody tests and the importance of accurate and reliable testing. However, we remain concerned that some recommendations in the current CDC antibody guidance are not rooted in the most up-to-date scientific evidence on the use of serologic tests.

Specifically, CDC's guidance states, "Serologic test results should not be used to make decisions about grouping persons residing in or being admitted to congregate settings, such as schools, dormitories, or correctional facilities. Serologic test results should not be used to make decisions about returning persons to the workplace." ACLA acknowledges that further research is necessary to better understand the interpretation of serologic test results as they relate to SARS-CoV-2 immunity. However, CDC's current guidelines are being interpreted by many providers, employers, occupational health personnel, and health plans to suggest that serologic test results have no utility in the management of individuals and populations in the workplace and congregate settings. As currently drafted, these guidelines contradict recent statements made by

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CDC officials regarding the intent of the antibody guidance. On a May 27 call with ACLA members, CDC officials stated that while there is not enough evidence to support the use of antibody tests as the sole factor for reopening or returning to work, antibody tests may be one factor to consider. This stated intent is logical, since it is more likely that a person who has developed an immune response to the SARS-CoV-2 virus has developed some greater degree of immunity (whatever it may be) than a person who tests negative for those antibodies. That likelihood would be worth considering, among other data, in making back to school and back to work decisions. However, the guidelines as drafted do not reflect this intent.

In addition, the definition of "return to work" in the current CDC guidance focuses only on those individuals who have been symptomatic and confirmed to have COVID-19 infection. But in the broader healthcare community and in the general public, "return to work" is aligned with the federal government's "Opening Up America Again" campaign with the focus on prevention and ongoing surveillance at the workplace. While we agree that serology testing should not be used to determine whether a previously symptomatic and lab-confirmed infected individual may return to a worksite, serology testing results do offer significant value in individual and population health management that molecular testing alone cannot deliver. Below are just some real-life examples from ACLA members' practices where such values are illustrated.

- In asymptomatic individuals who tested positive or indeterminate with a molecular test due to low viral burden (high Ct values on the RT-PCR assays), serology test results have helped identify the timing of the suspected infection (e.g., at the beginning of an infection vs. entering the recovery phase). Such information has contributed significantly to individual follow-up management when screening asymptomatic returning workers in "closed" manufacturing, office, entertainment/sports, and production sites. It also contributed in several contact tracing investigations to determine the source(s) and sequence of potential outbreaks at workplace and congregate settings. For example, a positive PCR with a negative serology result points to a very recent infection while an indeterminate PCR result with a positive serology result indicates a nearly resolved infection. This distinction has been crucial when assessing employees with critical or irreplaceable roles in their organizations. It also has aided in contact tracing in congregate settings by helping focus resources.

- An individual's SARS-CoV-2 IgG serology result reflects the person's cumulative exposure history (up to 14 days prior to administering the test). Human studies have demonstrated that an individual may develop a protective/neutralizing antibody response within a week after PCR confirmation of SARS-CoV-2 infection. The population seroprevalence within an organization can be used as proxy for a group's past exposure history. Such individual and population pandemic history can aid in the assessment of the groups' past and ongoing exposure risks and help determine the most effective ongoing monitoring strategies and approaches, including whether to use surveillance testing, what testing modalities, and the frequency and scope of testing that should be considered in the population surveillance efforts. While we are still far away from

herd immunity for any given population, a shield immunity model can be created using those who recovered from infection with demonstrable antibody to reduce contact opportunities between susceptible and infectious individuals.

Further contributing to public misunderstanding of serology, the CDC Interim Guidelines for COVID-19 Antibody Testing uses hypothetical test performances to illustrate the value of orthogonal testing approaches, which implies that most serology tests are of little to no clinical value. The theoretical illustration of a positive predictive value benefit from orthogonal testing is not based on real-life experiences with high complexity commercial assays that have extremely high precision on repeat testing, and false negative and false positive tests are not random events. There are also practical concerns in offering orthogonal testing approaches. ACLA members and experts in laboratory medicine would welcome the opportunity for ongoing dialogue with the CDC in formulating future guidance on these topics.

Now more than ever, healthcare providers, health plans, businesses, and the general public are turning to CDC for clear guidance on the COVID-19 response. COVID-19 molecular testing, while extremely important in establishing a diagnosis in managing an acute illness episode, does not reflect past exposure history or provide any insight in future management in congregant settings. Serology does provide additional value in clinical and population health settings, particularly with the use of laboratory-based commercial assays with excellent sensitivity and specificity performance as published by the FDA.

We understand that CDC plans to update its antibody guidance based on the availability of new information. We urge CDC to take immediate steps to modify this guidance to reflect current scientific evidence and clarify the appropriate use of antibody testing as one factor, among several, in reopening decisions. In doing so, CDC can help ensure that antibody testing is accessible for Americans as an important tool in the public health response to COVID-19.

Thank you for your leadership on this critical matter. We remain committed to strengthening our public-private partnership and will continue to do everything we can to support the agency's COVID-19 response efforts.

Sincerely,

Julie Khani
President