COVID-19 Serology Applications – Summary of CPHLN Forward Plan

Coronavirus disease (COVID-19) caused by SARS-CoV-2 has rapidly evolved into a global pandemic. Front line diagnostic testing to identify acutely infected patients relies upon nucleic acid testing platforms which detect genomic material of the virus.

Additionally, antibody-based testing will be essential for understanding the dynamics of the immunological response to virus infection, and accordingly will play a key role in a number of public health applications. Based on the published literature, serological assessment of patients between 2 to 4 weeks after infection can potentially confirm whether an individual had been infected with SARS-CoV-2 the virus responsible for COVID-19 disease. However, at the present time the full immune response to SARS-CoV-2 infection is not well understood. Serology testing approaches are now being developed to support:

Assessment of SARS-CoV-2 seroprevalence: This information is epidemiologically important because being able to determine the prevalence of symptomatic and asymptomatic infections in Canada will be necessary to determine the denominator of infected Canadians in various jurisdictions (indicator of transmission rates). This information is critical to determine the spectrum of clinical infections associated with SARS-CoV-2 and to estimate what might occur when physical distancing measures are loosened.

Assessment of sero-immunity of front line workers: At present there is limited information with regard to an individual's immune status after COVID-19 infection. A very limited study in rhesus macaques suggests that infection may lead to immunity after COVID-19 infection. This has not been confirmed in humans, and the nature and duration of sero-immunity to SARS-CoV-2 is unknown. However, infections with other coronaviruses has been shown to induce neutralizing antibodies, and lead to sero-protection. Given the challenges in maintaining a protected workforce during the pandemic, the ability to assess prior exposure and potential sero-immunity in health care workers and other front line workers would be reassuring to personnel and policy makers.

Relationship to diagnostic approaches: Nucleic acid detection provides definitive confirmation of clinical COVID-19 infection, and detection of viral RNA is possible at the time of symptom onset. Conversely, based on the published literature it may take 3 to 7 days before an individual infected with SARS-CoV-2 produces sufficient IgM antibodies to be detected by a serological test. During this initial window period, individuals may be serologically negative, and be highly infectious. **Therefore, at the present time we do not support the use of SARS-CoV-2 serology as a diagnostic tool.** However, serology may be useful to develop targeted diagnostic testing strategies in which priority would be given to populations with low levels of immunity.

Testing approaches: A number of different serological platforms (see Appendix) are becoming available to detect SARS-CoV-2 antibodies; however, most of the commercial assays have not been fully validated for use. The goal of this study is to establish a panel of well-characterised serum samples so that the performance characteristics of these newly available diagnostic platforms can be evaluated. We propose that having serological tests which have sensitivities in >90% range at 2 weeks post symptom onset and specificities in the >98% range would assist in performing epidemiological studies and the assessment of potential sero-protection in front line workers which are necessary to support Canada's overall public health response to COVID-19. In this developmental process it will be important to

investigate the specificity of SARS-CoV-2 assays, including potential cross reactivity to other endemic coronaviruses such as HKU1, NL63, OC43, or 229E.

Appendix (summary of serology platforms):

a. Neutralisation assays are the gold standard for serological testing. They require specialised laboratory containment facilities (containment level 3) and highly trained personnel because they involve working with live cultures of the virus of interest. Although there may be some cross reactivity amongst closely related viruses, for the most part, neutralisation assays can differentiate antibody responses to specific viruses (e.g., SARS-CoV-1 vs SARS-CoV-2). Commercial assays like ELISAs or RTC may not have this level of discrimination and this feature is what makes neutralisation assay the "gold standard" for antibody detection and evaluation of other serological platforms.

b. ELISA are one of the most frequently used platforms for serological diagnosis. They are considered high throughput assays because most utilise a 96-well plate format; many are automated and as are result, results are available relatively rapidly. There are a limited number of commercial ELISAs that have been developed for detection of antibodies against SARS-CoV-2 but the number of assays entering the marketplace is rapidly expanding. Our goal is to work with a number of PPHL and hospital labs to evaluate the performance of a number of these assays.

c. Rapid test cassettes sometimes referred to as Point of Care (POC) tests have significant technological advantages over ELISAs. They are easy to use, do not require specialised equipment or expertise and have very rapid turnaround times (10-15 minutes). Most can detect IgM and IgG separately or in combination and if accurate, these assays could play a role in management of the COVID-19 pandemic. Unfortunately, the performance of these assays has rarely been evaluated on a large scale but we plan to evaluate a number of these antibody detection assays.