

## Ordering and Use of COVID-19 Serology Testing

Recognizing that there are a small number of specific clinical applications for this test (see below) and to alleviate any confusion between serology and the diagnostic PCR test, UVMHC will send IgG serology testing out to our reference lab partner Mayo Clinical Labs but only after pathology approval for the testing.

### Guiding Principles on Use of COVID-19 Serology:

1. Antibody testing is useful for:
  - a. Understanding how many people COVID-19 has infected (i.e., epidemiology studies, not a clinical application).
  - b. Identifying children presenting with Pediatric Multi-System Inflammatory Syndrome associated with COVID-19.
  - c. Assessing COVID-19 convalescent plasma donors.
2. Antibody testing should not be used to acutely diagnosis COVID-19 infection.
3. Antibody testing results should not be used to determine a person's COVID-19 immunity status, "return-to-work" decisions, use of masks or other personal protective equipment (PPE), or safety of vulnerable persons to go into public more.
4. A positive antibody test only tells you that an individual has been infected with COVID-19 in the past.
5. Antibody testing results should be interpreted in terms of PPV, being mindful of the prevalence of COVID-19 in your particular community and the FP rate of any given test

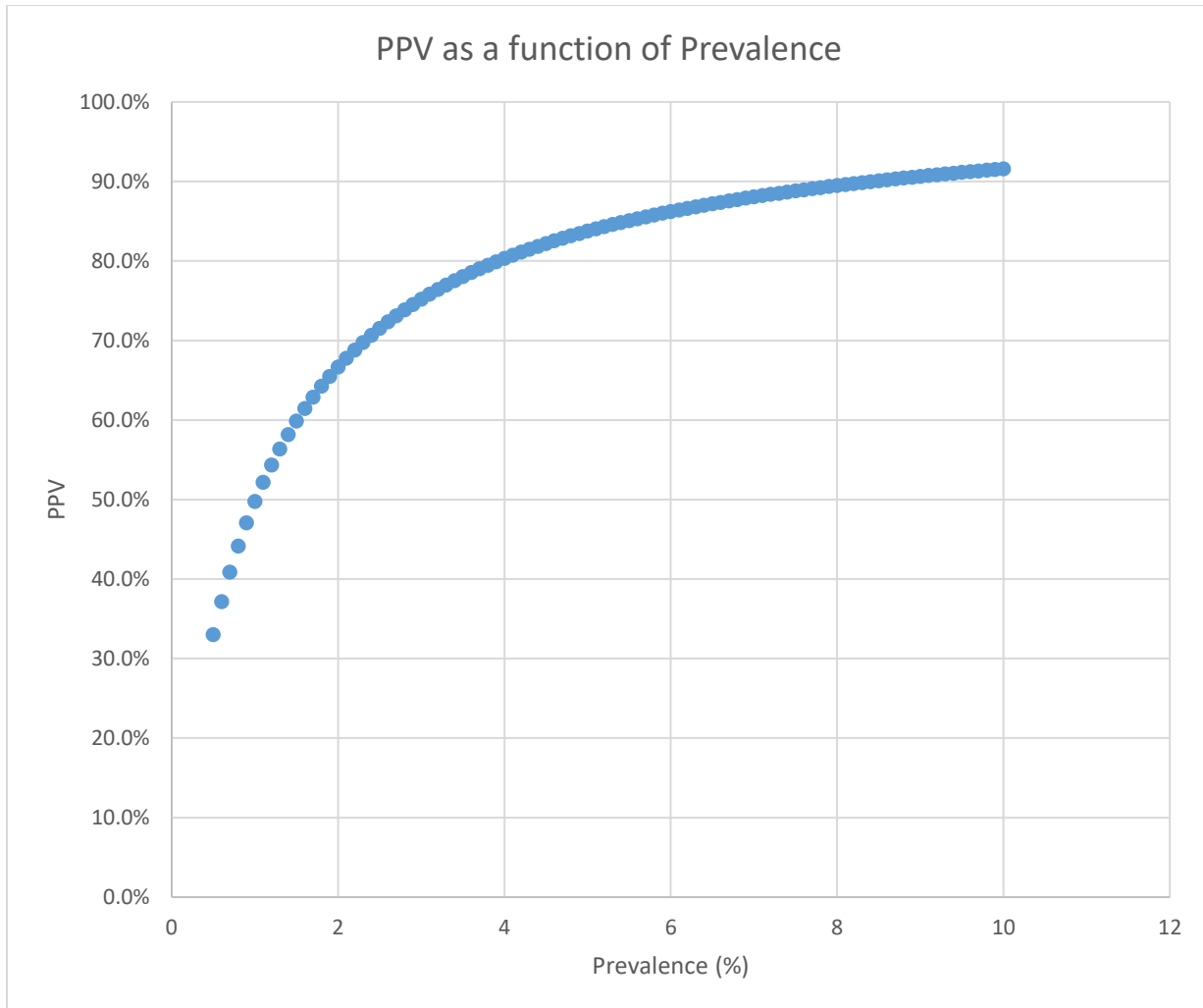
### Supporting Information and Rationale:

There has been much discussion in the media and lay press on the use of serology (antibody) testing in combating the COVID-19 pandemic. Some of this information has been misleading and promises unrealistic expectations on how the testing can be used to "re-open" the economy and identify a person's COVID-19 immunity status. This letter is to provide you with realistic expectations on the use and limitations of COVID-19 serology testing in our community.

Depending on the type of serologic test, the assay may detect IgM antibodies, IgG antibodies, or both. In general, IgM antibodies are less specific, leading to higher rates of cross-reactivity and false positives. Therefore, IgG should be the primary antibody measured for COVID-19 serology. The sensitivity of the serology assays is dependent on the length of time that has elapsed since symptom development. In patients who have only had symptoms for less than 5 days, sensitivity can range between 0-25%. Sensitivity improves the longer it has been since symptom onset, with 92-100% sensitivity observed in patients tested after 14 days.

There is a general expectation that a positive antibody test to COVID-19 would suggest some immunity to future infection by the virus. Unfortunately, it is too early in our knowledge of COVID-19 to know if antibodies are protective, how long they last, or how they may impact an individual's ability to infect others. Early data suggests that the development and the effectiveness of these antibodies may depend on an individual's age, overall health, and the severity of his/her COVID-19 related illness. In general, those of older age and greater severity of COVID-19 illness are more likely to have developed antibodies in response to COVID-19 infection.

Another factor that complicates using COVID-19 serology, and any laboratory test for that matter, is the risk of a false negative or false positive result. The positive predictive value (PPV), or likelihood that the positive test result is correct (a "true positive"), is driven by the disease prevalence in combination with the test specificity, or rate of false positive results ( $FP = 1 - \text{specificity}$ ). For COVID-19, the assumed prevalence in Northern NY and most of VT is around 1%. The FP rate with even the "best" COVID-19 serology test is 1%. To calculate PPV you divide the prevalence by prevalence plus the FP rate. So a patient who lives in Northern NY or most areas of VT, has a 50/50 chance (coin flip) their positive result is actually a true positive. If the prevalence of COVID-19 is less than 1%, such as in the Northeast Kingdom of VT, or in the case of a "worse" serology test with a higher FP rate, the PPV can decrease to 17% (rolling a 1 on 6-sided dice) or less. Below is a graph of PPV as a function of prevalence for a test with 98% sensitivity and 99% specificity.



Sincerely,

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