PROJECT COVERED

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RE: Test Result Interpretation

Dear Project COVERED Participant:

Thank you for participating in Project COVERED. We are excited to have such a motivated group of health care professionals who have agreed to participate to help us learn how to reduce the risks of COVID-19 transmission to health care workers.

As you know, you are being tested for COVID-19 viral shedding and seroconversion as part of this project. *Viral shedding* is being tested by taking a sample of secretions from your nose through a self-inserted nasal swab. This swab will be tested for the presence of viral particles. *Seroconversion* is testing whether your body has created antibodies to SARS-CoV-2, the virus that causes COVID-19 illness. This test is done by collecting a blood sample. These antibodies are created after your body has fought the COVID-19 viral infection, and some of these antibodies typically persist after recovery. These tests are measuring different aspects of infection and exposure, and both will be helpful in learning who has been exposed to COVID-19 and who develops infection. We are still learning a lot about COVID-19, but some people develop the infection without symptoms, so collecting these specimens every 2 weeks is a really important factor in learning how we protect front-line health care workers from COVID-19 acquisition.

Unfortunately, these tests are not perfect. The purpose of this letter is to provide you details of the performance of the tests we are using, to help you understand your test results. If you end up testing positive for COVID-19, you will need to contact your employee health clinic immediately — providing this letter will help them guide you on next steps.

Nasal Swab Testing

The testing you have undergone is from a self-inserted nasal swab. This swab is tested for SARS-CoV-2 virus particles. This testing is similar to what you might undergo if you have symptoms consistent with COVID-19. Self-inserted nasal swabs are less invasive than clinician-inserted nasopharyngeal swabs, and they are currently thought to have similar sensitivity. This test has received an Emergency Use Authorization (EUA) from the FDA, but no current SARS-CoV-2 viral tests have received FDA approval. Testing for the purpose of this project was conducted by ARUP Laboratories.

It is unclear how good this test is in people who have no symptoms of COVID-19. This test is very specific for detecting virus particles. It is possible, however, that the test may not detect the virus if you are very early in the course of disease or you are shedding a very low level of virus. Because of this, the test manufacturer notes several limitations of this test:

- Negative results do not preclude SARS-CoV-2 infection and should not be used as the sole basis for patient management decisions;

- Negative results must be combined with other clinical observations, patient history, and epidemiologic information;
- A positive result indicates the detection of nucleic acid from the relevant virus;
- Nucleic acid may persist even after the virus is no longer viable;
- Positive results do not rule out bacterial infection or coinfection with other viruses; and
- Reliable results are dependent on adequate specimen collection, transport, storage, and processing.

Blood Sample Testing

The testing you have undergone is serology testing for anti-SARS-CoV-2 IgG. That means we are testing your blood for antibodies against SARS-CoV-2. You would develop those antibodies if you have been exposed to the virus. This may happen when you have clinical (symptomatic) COVID-19 infection, or you may have been infected but not developed symptoms. While this testing means you have antibodies indicating previous infection, we do not currently know whether the presence of these antibodies confers immunity (i.e., protects you from re-infection), or how long those antibodies will stay in your body.

The antibody testing performed on your blood uses the Abbott anti-SARS-CoV-2 IgG test. This test only tells us whether antibodies are DETECTED or NOT DETECTED. The ability of this test to detect antibodies depends on how long it has been since you were exposed. In a cohort of people with normal immune systems who had COVID-19 infection, 86% of people had a positive test between 8 and 13 days from the onset of symptoms, and 100% of people had a positive test 14 days after symptom onset. Among those who did NOT have COVID-19, 99.6% of them had a negative test. This test has received an Emergency Use Authorization (EUA) from the FDA, but no current anti-SARS-CoV-2 antibody tests have received FDA approval. Testing for the purpose of this project was conducted by ARUP Laboratories, and used the Abbott test.

Because the test is not perfect, the test manufacturer notes several limitations of this test:

- Antibody test results should not be used as the sole criterion to confirm or rule out SARS-CoV-2 infection or to assess infection status;
- Negative results do not exclude infection with SARS-CoV-2, especially in individuals with known exposure to virus;
- Follow-up molecular diagnostic testing should be considered in those with known exposure to COVID-19;
- Immunocompromised patients infected with COVID-19 may have a delayed antibody response or antibody levels too low to result in a positive test; and
- Positive results suggest exposure to SARS-CoV-2 but do not indicate immunity. Past or current infection with non-SARS-CoV-2 coronavirus strains, including HKU1, NL63, OC43, or 229E, can cause false-positive results

For the purpose of this project, any tests that yield a positive result on the Abbott test will be confirmed using another antibody assay, the Euroimmun test. This test provides both a qualitative

interpretation and a quantitative interpretation, and is also performed by ARUP Laboratories. The ratio-based quantitative result is classified as follows:

Ratio < 0.8	Negative
0.8 ≤ Ratio <1.1	Borderline/Indeterminate
Ratio ≥ 1.1	Positive

The Euroimmun assay may yield different results from the Abbott assay. In a cohort of people who had COVID-19 infection, only 33% had a positive test within 10 days of symptom onset. In a cohort who developed symptoms of COVID-19 at least 10 days before testing, 80% had a positive test. Among blood samples known not to have COVID-19 infection, 98.5-99.0% of samples had a negative test (specificity).

If your blood test is negative by the Abbott test, only a single negative result will be reported to you. If your blood test is positive by the Abbott test, then both the Abbott and the Euroimmun test will be reported.

If you test negative…

Because we are testing health care workers who do not have symptoms, most people will have negative tests. That negative test does not *necessarily* mean that you do not have COVID-19 infection, but a negative test *in a person with no symptoms* means that you *probably* are not shedding viral particles *right now*. If you were to develop symptoms consistent with COVID-19 infection in the future (fever, cough, sore throat), however (even the day after testing), you should contact your local employee health clinic for evaluation. Repeat testing may be performed.

If you test positive with the nasal PCR test…

If you test positive for COVID-19 with the nasal test, you may be shedding SARS-CoV-2 virus. You should immediately contact your employee health clinic, and you should isolate yourself from others, wear a mask if you are not isolated, and you should not work clinically until cleared by your employee health clinic. If you are having no symptoms, some institutions may recommend repeat testing and/or work schedule modifications.

If you test positive on your blood test (serology)…

If you test positive for COVID-19 with the blood test (serology), you may have been exposed or infected with COVID-19 previously. You should immediately contact your employee health clinic while you isolate yourself from others and wear a mask if you are not isolated. You should not work clinically until cleared by your employee health clinic. If you have recently seroconverted (developed a positive test), you may have active COVID-19 infection, or you may have had a previous infection that you have cleared. If you have no symptoms, some institutions may recommend repeat viral (nasal or nasopharyngeal) testing and/or work schedule modifications. We do not currently know if you are immune to subsequent COVID-19 infection.

Test results will be reported through the electronic Case Report Form system, and you will be notified of new results by e-mail and text message. If you have a positive result, you may be notified by your local study coordinator or site PI additionally. Once provided the results, it is your

responsibility to obtain follow-up evaluation with your doctor, employee or occupational health clinic. Once you have both a positive Abbott and EuroImmun test, your blood tests and nasal swabs required and provided by the project will stop—no further specimens will be required. We appreciate your continuing to complete surveys, however.

Thank you again for participating in Project COVERED!

Sincerely,

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