Technical Alert

Possible False Positive SARS-CoV-2 (COVID-19) PCR

TO: Medical Staff, Clients, and Medical Laboratories

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SUBJECT: Cepheid GeneXpert and BD Max Instruments may be Reporting False Positives

Many companies are producing high quality SARS-COV-2 molecular tests under FDA Emergency Use Authorization (EUA), however, even high quality assays are not infallible. These COVID-19 testing methods were validated, implemented, and emergency approved in the US with less data and a shorter timeline than usual. As such, it is still not completely clear how many of these assays will truly perform in the field. Based on early experience with the GeneXpert and BD Max, there are concerns that these instruments are occasionally overcalling background signal as a positive result. Since implementation, we have identified suspect results at 4 of our 5 testing locations. Occurrences have been observed on GeneXpert 4 times and on BD Max 10 times. All of these were negative upon confirmatory testing and/or resubmission testing.

Each assay has a minimum of 2 target sequences, with internal fluorescent probes for real time detection. The primers and probes are designed to be specific with little to no cross reactivity to other respiratory flora or pathogen sequences, including SARS and MERS, and match SARS-COV-2 (COVID-19) sequences.

The instruments are presently set by the manufacturer to interpret a single target positive with very poor amplification efficiency (high Cycle Threshold [Ct] and/or atypical curve) as "DETECTED". None of these to date have confirmed positive when tested on other systems using similar targets, and may be a false positive due to background noise.

To ensure we provide the most accurate results we can, DLS has implemented a mandatory audit of all positive results from all systems. This includes an assessment of individual target reactions (genetic target) and efficiency (Ct values and reaction curve, if available). If any test hits only one of two targets OR if any Ct value is >40, then a preliminary result of "Presumptive Positive" is reported to ensure patients can be triaged conservatively and efficiently to minimize possible exposures. Confirmation testing is expedited either in-house or sent to the DOH State Laboratories.

Following confirmation, the "presumptive" result will be amended to a final "DETECTED" or "NOT DETECTED" result. In the case where the initial presumptive positive result is determined to be a false positive, and a final negative result is released, the ordering physician, institution, and infection control will be notified.

As more data regarding the performance of all the various methods become available, we will continue to update our community and make adjustments to our protocols and processes to ensure we provide the most accurate results possible to guide appropriate patient care.

If you have any questions, please call Dr. Amy Woron at 441-5436 or DLS client services at 589-5101.