HOLOGIC®

October 7, 2020

Subject: **Travel screening and return-to-work/school guidelines should be updated to include all FDA authorized NAATs including the Aptima SARS-CoV-2 Assay**

To Whom It May Concern,

Hologic has been notified by customers as well as domestic and international travelers that airline carrier and state/local COVID-19 emergency response managers are requiring negative test results with "Polymerase Chain Reaction (PCR) tests" in order to avoid being placed in quarantine for up to two weeks prior to traveling freely in the destination as well as to be cleared to return to workplace and school settings.

As of the date of this letter, over 263 nucleic acid-based amplified tests (NAATs), also called molecular IVD tests, from commercial manufacturers and clinical laboratories have been authorized by the United States Food and Drug Administration (FDA) for emergency use detection of SARS-CoV-2 nucleic acids[1,2]. While the vast majority of these tests utilize PCR or real-time PCR technology, a number of authorized NAATs utilize technologies other than PCR. These include the Aptima SARS-CoV-2 Assay, which employs Transcription Mediated Amplification (TMA), as well as others utilizing sequencing or other isothermal amplification and chemiluminescent detection methods. **Given the established performance, authorized claims, and approximately 20% market share of commercial molecular SARS-CoV-2 testing for the Aptima SARS-CoV-2 Assay in the United States, we believe travel screening and return-to-work/school guidelines must be updated to include all FDA authorized NAATs, including the Aptima SARS-CoV-2 Assay, as updated in real time at FDA's website[2].**

[1] Food and Drug Administration, CDRH COVID-19 Daily Round-up, https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-daily-roundup-september-30-2020?utm_medium=email&utm_source=govdelivery, last accessed September 30, 2020

[2] Food and Drug Administration webpage for In Vitro Diagnostics EUAs, https://www.fda.gov/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/vitro-diagnostics-euas, last accessed September 28, 2020.

NAATs are molecular amplification methods and are distinctly different from serology (antigen or antibody) tests. An antibody test is designed to detect an immune response from a current or prior infection and cannot be used on its own to diagnose a current infection. These are distinctly different from rapid antigen tests, which are designed to detect viral antigens and diagnose acute infection, but which do not utilize amplification technology for increased sensitivity. Information about the different tests authorized for emergency use can be found on FDA's website[1].

In the following sections, we provide an overview of authorized intended use, regulatory status, performance and current market share for the Aptima SARS-CoV-2 assay. We believe this information justifies the requested modification to travel screening and return-to-work/school guidelines during the COVID-19 pandemic.

Abbreviated Intended Use

The Aptima SARS-CoV-2 assay is a nucleic acid amplification *in vitro* diagnostic test intended for the qualitative detection of RNA from SARS-CoV-2 isolated and purified from upper respiratory specimens (such as nasopharyngeal (NP), nasal, mid-turbinate and oropharyngeal (OP) swab specimens and nasopharyngeal wash/aspirate or nasal aspirates) obtained from individuals meeting COVID-19 clinical and/or epidemiological criteria, as well as upper respiratory specimens (such as nasopharyngeal, nasal, mid-turbinate or oropharyngeal swab specimens) collected from any individual, including from individuals without symptoms or other reasons to suspect COVID-19 infection. The test is also for the qualitative detection of SARS-CoV-2 RNA in pooled samples containing up to 5 individual upper respiratory swab specimens. The Aptima SARS-CoV-2 assay is for use only under Emergency Use Authorization (EUA) in US laboratories certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, that meet requirements to perform high complexity tests.

The current FDA Letter of Authorization with complete intended use and claims is included with this letter.

Regulatory Status

The **Aptima SARS-CoV-2 assay** is CE-marked and it is also approved/authorized in the following geographies: USA, Australia and New Zealand, Canada, India, Israel, Japan, Singapore, India, Saudi Arabia, and Zambia. Evidence of approval by regulatory authorities can be provided upon request.

Performance with the FDA SARS-CoV-2 Reference Panel and Commercial Panels

As a condition of the EUAs for molecular IVD assays intended to detect SARS-CoV-2, FDA required EUA holders for NAATs to complete testing with the FDA SARS-CoV-2 Reference Panel. Testing with the panel allows for a more precise comparison of the analytical performance of different molecular IVD assays intended to detect SARS-CoV-2 nucleic acids. The Reference Panel contains common, independent, and well-characterized reference material. Hologic's Aptima SARS-CoV-2 assay demonstrated a limit of detection of 600 NDU/mL (NAAT Detectable Units/mL), which was among the best in the survey, out-performing most PCR-based tests. **Comparative results from all of the participating EUA holders is posted on FDA's website**[3].

The Aptima SARS-CoV-2 assay, which utilizes TMA chemistry, performs similarly to the Panther Fusion® SARS-CoV-2 assay, which is a RT-PCR assay. The analytical sensitivity of the Aptima and Panther Fusion SARS-CoV-2 assays was evaluated using reference material from three commercial vendors. Serial dilutions of the reference material were made in STM and 20 or more replicates at each level were tested using each of two assay reagent lots across two Panther/Panther Fusion systems. The reference materials and the lowest dilution levels resulting in ≥ 95% detection are listed in **Table 1**.

[3] Food and Drug Administration webpage for SARS-CoV-2 Reference Panel Comparative Data, https://www.fda.gov/medical-devices/coronavirus-covid-19-and-medical-devices/sars-cov-2-reference-panel-comparative-data, last accessed September 28, 2020.

Table 1: Analytical Sensitivity Evaluation of Commercial Reference Material

Vendor	Name	Reference #	Lot #	Analytical Sensitivity	
				Aptima SARS-CoV-2 Assay (TMA)	Panther Fusion SARS-CoV-2 Assay (PCR)
Zeptometrix	SARS-CoV-2 External Run control	NATSARS (COV2)-ERC	324332	83 Copies/mL	194 Copies/mL
SeraCare	AccuPlex SARS-Cov-2 Reference Material	0505-0126	10483977	83 Copies/mL	194 Copies/mL
Exact Diagnostics	SARS-CoV-2 Standard	COV019	20033001	83 Copies/mL	83 Copies/mL

Market Share and Number of Tests Performed

The Aptima SARS-COV-2 assay is run on Hologic's Panther system. There are more than 1,200 Panther systems installed in the United States and the test is run in approximately 400 US laboratories across all 50 states. With more than 25 million tests shipped to US laboratories, the Aptima SARS-CoV-2 assay represents a significant portion of the US molecular testing supply since the COVID-19 pandemic began.

The Aptima SARS-COV-2 assay is also the most predominant high-throughput test currently in use by Public Health laboratories across the U.S. The Associating of Public Health Laboratories (APHL), in their weekly surveys of Public Health response to COVID19, notes that Public Health laboratories in the U.S. are using more Aptima SARS-COV-2 assays than any other available test except for the CDC 2019-nCoV RT-PCR Panel[4].

Summary

In summary, the Aptima SARS-CoV-2 test is a NAAT that is one of the few authorized by the FDA for use in asymptomatic testing. Test performance is comparable to or better than PCR-based tests, which is evidenced by results from the SARS-COV-2 reference panel and evaluation with other commercially available reference materials. The Aptima SARS-CoV-2 assay has been registered in many countries and has a significant geographic footprint. Since its launch in May 2020, Hologic's Aptima SARS-CoV-2 assay has been used to test tens of millions of

[4] Association of Public Health Laboratories (APHL) Lab Testing Capability and Capacity Survey Data Dashboard https://www.aphl.org/programs/preparedness/Crisis-Management/COVID-19-Response/Pages/COVID-19-Dashboard.aspx, last accessed October 1, 2020

patients in the United States and will continue to serve a large population of patients and travelers in the US and abroad. The authorized intended use, assay principles, performance, regulatory status, and current market share for the Aptima SARS-CoV-2 assay easily warrant modification of the language regarding the types of technologies used to allow individuals to clear travel restrictions and return-to-work/school programs during the COVID-19 pandemic. **Accordingly, Hologic respectfully requests that travel screening and return-to-work/school guidelines be updated from "PCR" tests to include all FDA authorized NAATs for detection of SARS-CoV-2.**

Additional details regarding performance of the Aptima SARS-CoV-2 assay can be found in the Package Insert which is posted online at www.hologic.com.

Should you have any questions or concerns about this information, please contact Hologic Customer Support by telephone 1-800-442-9892 or by email: customersupport@hologic.com.

Sincerely,

Kevin Thornal
Division President, Diagnostic Solutions
Hologic, Inc.