Maryland
DEPARTMENT OF HEALTH

Minutes of Meeting – November 20, 2020

The Laboratory Advisory Committee (LAC) Emergency meeting took place by conference call at 2:30 p.m.

Members Attending: John G. Newby, Chair, American College of Pathology
Piyush K. Patel, Vice Chair, American College of Physicians
Barbara S. Caldwell, American Society of Clinical Pathology
Melissa Day-Ye, Consumer Member
Lindsey Howard, Jr., Industry
Gail McGucken, Laboratory Surveyor Scientist II, OHCQ
Gattu Rao, Maryland Academy of Family Physicians
Thomas J. Remsberg, Pharmacist

Other Attendees: Dr. Robert Myers, Director, Laboratories Administration
Rodney Hargraves, Deputy Director, Administrative and Support Services
Renee Scurry, Administrator, Regulatory and Administrative Services
Hope Miller, Paralegal II, Regulatory and Administrative Services
Paul Celli, Public Health Administrator, OHCQ

Members Absent: None

Cepheid Attendees: Meghan Lawson, Senior Manager, Market Access and Reimbursement Strategy, Government Affairs
Michael J. Loeffelholz, Ph.D., ABMM, Senior Director of Medical Affairs
Michele Schoonmaker, Vice President Government Relations and Public Policy
Angela Stewart, Senior Director, Government Relations and Public Policy
Whitley Quan, State Health Policy Analyst, Government Affairs

I. Cepheid's Xpert® Xpress SARS-CoV-2, Flu A, Flu B, RSV four-in-one test (in which Cepheid is seeking a letter of exception for use post EUA).

Background

The Laboratory Advisory Committee ("LAC") received a request from The Maryland State Medical Society (MedChi), which was forwarded on behalf of Cepheid (a molecular diagnostics company) and received by former Secretary Robert R. Neall. In their letter, MedChi requested the LAC to grant a Letter of Exception for Cepheid's Xpert® Xpress SARS CoV-2, Flu A, Flu B and RSV combination test.

In response, the LAC held an emergency conference call meeting to review this request. Cepheid was given an opportunity to provide a 5 minute presentation on the Xpert® Xpress SARS CoV-2, Flu A, Flu B and RSV combination test and thereafter participated in a brief question and answer session.

Presentation by Michael Loffelholz of Cepheid on the Xpert® Xpress SARS-CoV-2, Flu A, Flu B, RSV Four-In-One Test

Cepheid's Xpert® Xpress SARS-CoV-2, Flu A, Flu B, RSV four-in-one test combines COVID-19, Flu A, Flu B and RSV into one test. This four-in-one test is performed using respiratory swabs and washes. A cartridge is placed into an instrument for testing and results will be available approximately 25 to 30 minutes later.

The cartridge can be run on several different instruments for: (1) COVID, (2) Influenza A, (3) Influenza B and (4) RSV and gives a positive or negative result. In clinical trials, the four-in-one test had excellent performance and was found to have better sensitivity than other individual tests.

The four-in-one test (which is performed with a single step specimen collection) has a one cartridge design for the complete test menu and has a variety of instrument options that can be used efficiently in point-of-care settings for continuity of care. The test is performed on directly collected specimens where the sample is placed into a cartridge and thereafter placed into an instrument. The cartridge design makes the test easy to perform and reduces contamination.

Question and Answer Session

Question: Dr. Newby stated that the Laboratory Advisory Committee previously considered Cepheid's methodology, but did not grant excepted status because the assay did not meet the Centers for Disease Control (CDC) requirements for testing in a hood or contained environment. Dr. Newby thereafter inquired how Cepheid would answer questions regarding the CDC's requirements?

Answer: Dr. Loeffelholz replied that the CDC and World Health Organization (WHO) has recognized that there are point-of-care COVID tests that are performed outside of lab settings; and testing can be performed outside of a BSL-2 laboratory if manipulations are simple enough to reduce risk.

Question: Ms. Barbara Caldwell asked if Cepheid could speak on the limitations listed on page 22 of the handout, i.e., *Section 18 – Limitations* from the EUA-Cepheid - Xpert® Xpress SARS-CoV-2/Flu/RSV PDF from Cepheid?

Answer: Dr. Loeffelholz replied that these are boiler plate limitation statements. As with any test, mutations can affect test results. The flu vaccine can affect results because it's a live vaccine. Possible beta corona virus could also affect test results, which is continuously being monitored.

Question: What is the likelihood of contamination from one test to the next? Do you have to change gloves between each sample?

Answer: Dr. Loeffelholz replied that environmental contamination is extremely rare. When collecting a specimen for the test, you open the container, put in the specimen, then the container is never opened again. Dr. Loeffelholz also recommends changing gloves and cleaning surfaces between each test.

Question: Ms. Melissa Day-Ye asked what training is offered? Is there customer service support?

Answer: Dr. Loeffelholz replied yes. It is a standard process. All customers receive initial training. Field service engineers are also available for customer training. In addition, training can be completed in one day, but this depends upon the users.

Question: Dr. Newby stated that the Laboratory Advisory Committee has special criteria for tests on the excepted test list, i.e. quality control and proficiency testing. This test would require both to

ensure that the test is functioning properly.

Answer: Dr. Loeffelholz replied that there are commercially available proficiency and quality control measures.

Mr. Paul Celli stated that the Xpert® Xpress SARS-CoV-2/Flu/RSV four-in-one test will fall under molecular biology PCR waived tests which requires proficiency testing, user manual information and documentation of training. Dr. Loffelholz thereafter stated that every cartridge has (1) internal controls where reagents are integrated into the cartridge to prevent false positives and (2) external controls which are reference materials that are commercially available and customers can add to the cartridge. Ms. Caldwell replied that internal controls are required, but external controls are not. Therefore, with no inspection process, what is the recommended frequency for running the test. Ms. McGucken responded that it is optional; and Dr. Loffelholz provided that most manufacturers do not provide external controls so users should be compliant with accreditation agencies on the local, State and federal level.

Dr. Newby then noted that if the FDA 510(k) premarket notification is refused for the Xpert® Xpress SARS-CoV-2, Flu A, Flu B, RSV four-in-one test, then the test will be removed from the excepted test list. Mr. Celli subsequently asked what the difference was between the four-in-one test and any other EUA test and Dr. Loffelholz replied that it will provide continuity of care. Mr. Celli then inquired whether the FDA would approve the test after the EUA ends since FDA review is now required for non-excepted tests. Dr. Newby agreed with Mr. Celli's assessment and inquired whether excepted test status has become moot.

As for risk, Dr. Myers is concerned with biosafety risk assessment and believes that biosafety guidance needs to be provided to users. Lastly, Dr. Newby ended the discussion by stating that any respiratory point-of-care medical service should require splash shields and personal protective equipment (PPE).

At the conclusion of the presentation, each LAC member was directed by Dr. Newby to send Hope Miller their vote by Monday, November 23rd. Members were instructed to respond with:

(1) Approved;
(2) Not Approved; or
(3) Approved with Conditions (e.g. proficiency testing and reporting requirements)

II. Adjournment

The meeting was adjourned at 3:17 p.m.

Respectfully submitted,

Renee Scurry and Hope Miller
MDH Laboratories Administration
Office of Regulatory and Administrative Services