08-24 New FDA Webpage on Pooled Sample Testing and Screening Testing

The U.S. Food and Drug Administration (FDA) has taken steps to encourage the development of tests for screening asymptomatic individuals and for testing pooled samples. Today, the FDA posted a new webpage that provides an overview of available resources related to SARS-CoV-2 screening testing and testing using pooled samples.

Pooled Sample Testing and Screening Testing for COVID-19

The FDA has taken steps to encourage the development of tests for screening asymptomatic individuals and for testing pooled samples, as summarized in the June 16, 2020, FDA Statement Facilitating Diagnostic Test Availability for Asymptomatic Testing and Sample Pooling. The FDA has continued to work with developers to facilitate testing of pooled samples, including providing more detailed recommendations in the July 6, 2020, and July 28, 2020, updates to the EUA templates.
This page provides an overview of available resources related to SARS-CoV-2 screening testing and testing using pooled samples.

On this page:

Overview

The FDA encourages developers to consider validating their tests for the screening of asymptomatic individuals and for testing pooled samples.

Resources

The FDA has provided these resources about testing using pooled samples and testing for asymptomatic screening:

- Emergency Use Authorization (EUA) Templates: Include validation recommendations for tests, including for screening of asymptomatic individuals and pooled sample testing.
- FAQs on Testing for SARS-CoV-2: Includes Frequently Asked Questions, including about screening of asymptomatic individuals and pooled sample testing, and discusses the differences between surveillance, screening, and diagnostic testing.

Pooled Sample Testing

The FDA is aware that there is a great interest in performing testing using pooled samples. Pooling samples involves mixing several samples together in a "batch" or pooled sample, then testing the pooled sample with a diagnostic test. This approach increases the number of individuals that can be tested using the same amount of resources. For example, four samples may be tested together, using only the resources needed for a single test. However, because samples are diluted, which could result in less viral genetic material available to detect, there is a **greater likelihood of false negative results**, particularly if not properly validated. This method of pooling samples works well when there is a low prevalence of cases, meaning more negative results are expected than positive results.

Validation

The FDA believes that sample pooling can be authorized for use in certain SARS-CoV-2 tests with appropriate mitigations and validation. The FDA has provided validation recommendations for tests intended for use with pooled samples in the EUA Templates. Test developers seeking authorization for their test for use with pooled samples should validate their test for such use, considering the validation recommendations outlined in the EUA templates, and submit an EUA request to the FDA.

As discussed in the templates, there are currently two approaches to patient specimen pooling:

- Sample/media pooling: Pooling aliquots of transport media each containing a single patient sample or
- Swab pooling: Adding swabs from multiple patients into a single volume of transport media.

The templates include validation recommendations for both types of pooling approaches.

Generally, the FDA recommends validating the test with either pooling approach in a way that preserves the sensitivity of the test as much as possible. That is, it is preferable to use an approach where all specimens identified as positive when tested individually are also identified as positive when tested using the pooled testing approach. However, a decrease in performance is likely with pooling strategies, due to dilution of the primary clinical sample.

As discussed in the templates, since sample pooling will greatly increase the number of individuals that can be tested using existing resources, a small reduction in sensitivity may be acceptable depending on the pooling efficiency and other mitigations in place. Therefore, the FDA generally recommends that, after pooling, test performance includes ≥85% percent positive agreement (PPA) when compared with the same test performed on individual samples. Additional limitations, such as considering negative results from pooled samples to be presumptive negatives, may be recommended based on the patient population included in the sponsor's clinical evaluation and the performance data submitted in the EUA request.

As discussed in the templates, a plan for ongoing monitoring of the positivity rate and of the performance of a test with a pooling strategy should be included in the test's

procedures. As data become available and new approaches are identified, our recommendations in these templates may evolve.

Testing Considerations

A Clinical Laboratory Improvement Amendments (CLIA) certified laboratory **using a test authorized for pooling** must follow the manufacturer's authorized Instructions for Use (IFU). Additionally, the Letter of Authorization issuing the EUA includes certain Conditions of Authorization, some of which apply to the authorized laboratories performing the test.

Generally, laboratories should report diagnostic or screening negative test results to the individuals in the pool according to the instructions for use or the EUA Summary of the FDA-authorized SARS-CoV-2 test that the laboratory used, including providing the associated Fact Sheet.

The test report given to the individuals in the pool should include any information specified in an EUA, such as indicating that the testing procedure involved specimen pooling and explaining the limitations of that type of testing.

As discussed in the CDC guidance, Interim Guidance for Use of Pooling Procedures in SARS-CoV-2 Diagnostic, Screening, and Surveillance Testing

- The CLIA-certified laboratory **must also report** those diagnostic or screening negative test results to appropriate federal, state, and local public health agencies in accordance with applicable federal, state, and local laws.
- The CLIA-certified laboratory **should not report** positive or indeterminate results of a pooled test to either the individuals in the pool, or the local, state, tribal, or territory health department. All individual specimens that were in a pooled test with a positive or indeterminate result should be retested separately, and the subsequent individual diagnostic or screening results must be reported to the local, state, tribal, or territory health department as well as to the individuals tested.

Screening of Asymptomatic Individuals

The FDA regulates screening tests as *in vitro* diagnostics (IVDs). Screening for COVID-19 systematically looks for individual infections in a group even if there is no reason to suspect those individuals are infected. Screening involves testing asymptomatic individuals who do not have known exposures with the intent of making individual decisions based on the test results. Screening tests are intended to identify infected individuals before they develop symptoms or to identify infected individuals who may not develop symptoms, so that measures can be taken to prevent further spread.

Examples of screening include testing, regardless of exposure or signs and symptoms, such as:

- An employer testing all employees returning to the workplace
- A school testing all students and faculty returning to the school.

In both examples, the intent of screening would be to use the results to determine who may return and what protective measures to take on an individual basis.

Laboratories may be interested in using pooling techniques when performing testing for screening of asymptomatic individuals, since this involves testing a large volume of patient samples. Additionally, pooling is most effective when there is a low prevalence of

cases, which may be more likely in an asymptomatic population, particularly if the population is at low risk for contracting COVID-19.

Validation

Screening using a highly sensitive test, especially given the asymptomatic testing population, leads to the most accurate results when rapid turnaround times are available. The FDA has provided validation recommendations designed to establish high sensitivity for tests intended for screening in the EUA Templates. We encourage developers who want to offer a less sensitive test for screening to discuss validation approaches with us.

Developers seeking authorization for their test for screening asymptomatic individuals should validate their test for such use, considering the validation recommendations outlined in the EUA templates, and submit an EUA request to the FDA.

Testing Considerations for Providers

Most currently authorized SARS-CoV-2 diagnostic tests are authorized for use on individuals suspected of COVID-19 by their healthcare provider. The FDA recognizes that the CDC has issued guidance related to screening—and that organizations may want to conduct screening—of asymptomatic individuals as part of a strategy to assure the safety of their employees, patients, students, and others. An asymptomatic individual may be suspected of COVID-19 by their healthcare provider for many reasons, including known exposure or working in a high-risk environment. Such use is within the authorized indications for use of tests for individuals suspected of COVID-19.
For healthcare providers who are ordering an authorized SARS-CoV-2 diagnostic test to be used off-label (outside the authorization) to screen asymptomatic individuals not suspected of having COVID-19, we recommend they consider the information below. Although the current available literature suggests that symptomatic individuals with COVID-19 and asymptomatic individuals without known exposure may have similar levels of viral genetic material, there is limited data on the distribution of viral loads in individuals with and without symptoms across demographics, different settings, and specimen types. Therefore, when screening asymptomatic individuals, healthcare providers should consider using a highly sensitive test, especially if rapid turnaround times are available. If highly sensitive tests are not feasible, or if turnaround times are prolonged, health care providers may consider use of less sensitive point of care tests, even if they are not specifically authorized for this indication (commonly referred to as "off label"). For congregate care settings, like nursing homes or similar settings, repeated use of rapid point of care testing may be superior for overall infection control compared to less frequent, highly sensitive tests with prolonged turnaround times.

If less sensitive tests, such as some rapid point-of-care tests, are used, healthcare providers should be aware of the performance of the tests and may want to consider different testing approaches, such as serial testing.

As discussed in the EUA Templates, use of tests in a general, asymptomatic screening population is generally intended to be used as part of an infection control plan, that may include additional preventative measures, such as a predefined serial testing plan or directed testing of high-risk individuals. "Negative" results should be considered as "presumptive negative" and healthcare providers should consider them in the context of clinical observations, patient history, and epidemiological information. Thus, if there is a significant new outbreak in a congregate care facility, or high clinical suspicion of an infection in an individual resident, a negative point of care test should be confirmed with

a highly sensitive molecular test (refer to CDC guidelines). It is not necessary to perform confirmatory high sensitivity molecular tests on individuals with negative antigen test or other point-of-care test results if they are obtained during routine screening or surveillance.

Surveillance Testing

The FDA generally does not regulate surveillance testing. Surveillance testing is primarily used to gain information about infection at a community or population level, rather than an individual level. Surveillance testing can involve testing a certain percentage of a specific population to monitor for increasing or decreasing prevalence or to determine the effect of community interventions such as social distancing. Surveillance for SARS-CoV-2 includes ongoing systematic activities, including collection, analysis, and interpretation of health-related data that are essential to planning, implementing, and evaluating public health practice. Surveillance testing is generally used to monitor for a community- or population-level occurrence, such as an infectious disease outbreak, or to characterize the occurrence once detected, such as looking at the incidence and prevalence of the occurrence.

- *Example:* a testing plan developed by a state public health department to randomly select and sample 1 percent of all individuals in a city on a rolling basis to determine local infection rates and trends

Please refer to the Centers for Medicare & Medicaid Services (CMS) and the Centers for Disease Control and Prevention (CDC) for information on conducting surveillance testing and reporting results.

Questions?

Contact the FDA at CDRH-EUA-Templates@fda.hhs.gov with specific proposals or questions about asymptomatic testing or pooled sample testing.