Interim Guidance for Use of Pooling Procedures in SARS-CoV-2 Diagnostic, Screening, and Surveillance Testing

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Note: This document provides guidance on the appropriate use of testing and does not dictate the determination of payment decisions or insurance coverage of such testing, except as may be otherwise referenced (or prescribed) by another entity or federal or state agency.

What is pooling?

Pooling—sometimes referred to as *pool testing*, *pooled testing*, or *batch testing*—means combining respiratory samples from several people and conducting one laboratory test on the combined pool of samples to detect SARS-CoV-2, the virus that causes COVID-19.

Why is pooling used?

Pooling allows laboratories to test more samples with fewer testing materials. It could be useful in scenarios like returning groups of workers to a workplace.

What happens if the pooled test result is negative?

If a pooled test result is negative, then all the samples can be presumed negative with the single test. In other words, all of the people who provided samples can be assumed to test negative for SARS-CoV-2 infection.

What happens if the pooled test result is positive?

If the pooled test result is positive, each of the samples in the pool will need to be tested individually to determine which samples are positive.

When should pooling be used?

Pooling should be used only in areas or situations where the number of positive test results is expected to be low—for example in areas with a low prevalence of SARS-CoV-2 infections.

Definitions of Diagnostic, Screening, and Surveillance Testing for SARS-CoV-2

Definition of Diagnostic Testing

Diagnostic testing for SARS-CoV-2 is intended to identify occurrence at the individual level and is performed when there is a reason to suspect that an individual may be infected, such as having symptoms or suspected recent exposure, or to determine resolution of infection. Examples of diagnostic testing include testing symptomatic individuals who present to their healthcare provider, testing individuals through contact tracing efforts, testing individuals who indicate that they were exposed to someone with a confirmed or suspected case of coronavirus disease 2019 (COVID-19), and testing individuals present at an event where an attendee was later confirmed to have COVID-19. The U.S. Food and Drug Administration's (FDA) FAQs on Testing for SARS-CoV-2 also address diagnostic testing for SARS-CoV-2.

Definition of Screening Testing

Screening tests for SARS-CoV-2 are intended to identify occurrence at the individual level even if there is no reason to suspect infection—e.g., there is no known exposure. This includes, but is not limited to, screening of non-symptomatic individuals without known exposure with the intent of making decisions based on the test results. Screening tests are intended to identify infected individuals without, or prior to development of, symptoms who may be contagious so that measures can be taken to prevent further transmission. Examples of screening include testing plans developed by a workplace to test its employees, and testing plans developed by a school to test its students, faculty, and staff. In both examples, the intent is to use the screening testing results to determine who may return and the protective measures that will be taken. FDA's FAQs on Testing for SARS-CoV-2 also address screening testing for SARS-CoV-2.

Definition of Surveillance Testing

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. Surveillance testing is used to gain information at a population level, rather than an individual level, and results of surveillance testing can be returned in aggregate to the requesting institution. Surveillance testing may sample a certain percentage of a specific population to monitor for increasing or decreasing prevalence and to determine the population effect from community interventions, such as social distancing. An example of surveillance testing is a plan developed by a state public health department to randomly select and sample a percentage of all individuals in a city on a rolling basis to assess local infection rates and trends. FDA's FAQs on Testing for SARS-CoV-2 also address surveillance testing for SARS-CoV-2.

Diagnostic or Screening Testing Using a Pooling Strategy

General Guidance

Laboratories certified under the Clinical Laboratory Improvement Amendments (CLIA) can use a specimen pooling strategy to expand SARS-CoV-2 nucleic acid diagnostic or screening testing capacity when using a test authorized for such use by FDA.

If a pooled test result is negative, then all specimens can be presumed negative with the single test. If the test result is positive or indeterminate, then all the specimens in the pool need to be retested individually. The advantages of this two-stage specimen pooling strategy include preserving testing reagents and resources, reducing the amount of time required to test large numbers of specimens, and lowering the overall cost of testing.

A pooling strategy depends on the community prevalence of virus, and pool size will need to be adjusted accordingly. CDC recommends that laboratories should determine prevalence based on a rolling average of the positivity rate of their own SARS-CoV-2 testing over the previous 7–10 days. Laboratories should use a standardized methodology or

calculator that factors in the sensitivity of the assay they are using and their costs of testing to determine when the positivity rate is low enough to justify the implementation of a pooling strategy. Laboratories should also understand and, where appropriate, communicate the limitations associated with pooled testing, which are described in greater detail below.

Regulatory Requirements for Pooling of Diagnostic or Screening Testing

FDA regulates in vitro diagnostic devices and has provided recommendations and information regarding Emergency Use Authorization (EUA) requests for COVID-19 diagnostic tests in the Policy for Coronavirus Disease-2019 Tests During the Public Health Emergency (Revised) ("Policy for COVID-19 Tests") and the EUA templates referenced in that policy. COVID-19 assays and test systems used for diagnostic or screening testing, including those used for pooling, must have received an EUA from FDA, and some are being offered under the policies described in FDA's Policy for COVID-19 Tests.

Any SARS-CoV-2 in vitro diagnostic device authorized by FDA for use with specimen pooling will be included on FDA's list of In Vitro Diagnostics EUAs. FDA has also outlined various policies in FDA's guidance regarding the use of COVID-19 tests prior to authorization. A laboratory that wishes to use pooling with a SARS-CoV-2 nucleic acid test assay would be expected to evaluate and validate the performance of an assay for a pooling strategy—recommendations for doing so are included in FDA's Policy for COVID-19 Tests, including the Molecular Diagnostic Template for Laboratories—and submit an EUA request to FDA. After a laboratory notifies FDA according to the policies in FDA's guidance, FDA does not intend to object to the laboratory performing the validated pooling strategy while submitting their EUA request and during FDA's review.

If the laboratory modifies that authorized assay by incorporating alternative components, including extraction methods, polymerase chain reaction (PCR) instruments, and software versions, the laboratory should evaluate and validate the performance of the component changes, and recommendations for doing so are outlined in Section IV.A.4. of FDA's Policy for COVID-19 Tests. For more information on FDA's policies and recommendations, please see FDA's Policy for COVID-19 Tests, including FDA's Molecular Diagnostic Template for Laboratories, and FDA's FAQs on Testing for SARS-CoV-2.

Laboratories that conduct diagnostic or screening testing for COVID-19 must also comply with Clinical Laboratory Improvement Amendments (CLIA) regulations. If at any time a facility intends to report patient-specific test results, it must first obtain a CLIA certificate and meet all requirements to perform testing. For more information, see the Centers for Medicare & Medicaid Service's (CMS's) summary of the CLIA regulations.

Reporting Pooled Diagnostic or Screening Testing Results to Health Departments

Public Law 116-136, § 18115(a), the Coronavirus Aid, Relief, and Economic Security (CARES) Act, requires "every laboratory that performs or analyzes a test that is intended to detect SARS-CoV-2 or to diagnose a possible case of COVID-19" to report the results to state, local, tribal, or territory public health departments. On June 4, 2020, the Department of Health and Human Services published guidance on COVID-19 Pandemic Response, Laboratory Data Reporting: CARES Act Section 18115 that specifies what additional data must be reported by laboratories along with COVID-19 diagnostic or screening test results.

A CLIA-certified laboratory that allows for pooling must report diagnostic or screening negative test results to the participants in the pool according to the instructions for use of the FDA-authorized SARS-CoV-2 in vitro diagnostic device that the laboratory used. The test report given to the individuals in the pool should indicate that the testing

procedure involved specimen pooling and explain the limitations of that type of testing. The CLIA-certified laboratory must also report those diagnostic or screening negative test results to the local, state, tribal, or territory health department.

The CLIA-certified laboratory should not report positive or indeterminate results of a pooled test to either the participants in the pool, or the local, state, tribal, or territory health department. All participant 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.

Limitations of Pooled Diagnostic or Screening Testing

Based on limited data, using a pooling testing procedure for SARS-CoV-2 has some limitations. In a pooling procedure, the laboratory cannot ensure the diagnostic integrity of an individual specimen because it is combined with other specimens before testing. Specimen integrity can be affected by the quality of swab specimen collection, which could result in some swabs having limited amounts of viral genetic material for detection. Inadequate individual specimens, including those with limited amounts of viral genetic material, might not be eliminated from the pooled specimen before testing. Even if each individual specimen in a pool is adequate, the specimens in a pooled procedure are diluted, which could result in a low concentration of viral genetic material below the limit of detection of a given test. These limitations mean that monitoring the prevalence of disease and properly validating the assay and the instrumentation are important to limit the potential for false-negative results. In general, the larger the pool of specimens, the higher the likelihood of generating false-negative results.

The prevalence of COVID-19 in a population also affects the efficiency of pooled testing strategies. In general, lower disease prevalence may enable a laboratory to use a larger optimal pool size. A recent study by the Nebraska Public Health Laboratory found that nucleic acid tests for SARS-CoV-2 reliably returned a positive result when one positive sample was mixed with four negatives, and could reduce the number of tests needed by >50% in certain scenarios (such as a COVID-19 prevalence of 5%). However, as the prevalence of COVID-19 increases, the cost savings of a pooling strategy decreases because more pooled tests will return positive results and those specimens will need to be retested individually.

CDC continues to pursue research studies on pooling strategies for testing for SARS-CoV-2 and will update this guidance as needed.

Surveillance Testing Using a Pooling Strategy

General Guidance

Surveillance testing can be conducted in a laboratory that has a CLIA certificate, or in a laboratory that does not have a CLIA certificate. In its Frequently Asked Questions: SARS-CoV-2 Surveillance Testing, CMS indicates (CMS FAQs: SARS-CoV-2 Surveillance Testing) that ***during the COVID-19 public health emergency and associated authorizations***, "facilities performing SARS-CoV-2 surveillance testing using a pooled sampling procedure to report ***non patient-specific*** SARS-CoV-2 cohort results will not require CLIA certification." FDA's FAQs on Testing for SARS-CoV-2 state that FDA generally does not regulate surveillance testing.

A specimen pooling strategy can expand a laboratory's capacity to conduct SARS-CoV-2 nucleic acid surveillance testing. If a pooled test result is negative, then all specimens can be presumed negative with the single test. If the test result is positive or indeterminate, then all the specimens in the pool need to be retested individually. The advantages of this two-stage specimen pooling strategy include preserving testing reagents and resources, reducing the amount of time required to test large numbers of specimens, and lowering the overall cost of testing.

A pooling strategy should only be used when the prevalence of COVID-19 is low. CDC recommends that laboratories should determine prevalence based on a rolling average of the positivity rate of their own SARS-CoV-2 testing over the previous 7–10 days. Laboratories should use a standardized methodology or calculator that factors in the sensitivity of the assay they are using and their costs of testing to determine when the positivity rate is low enough to justify the implementation of a pooling strategy. Laboratories should also understand the limitations associated with pooled testing, which are described in greater detail below.

Assays and Test Systems for Pooling of Surveillance Testing

Although FDA generally does not regulate surveillance testing, CDC recommends that laboratories conducting surveillance testing with pooling should use an assay and test system that has received an EUA from FDA. Using an FDA-authorized assay and test system helps ensure the quality and reliability of testing. FDA authorized SARS-CoV-2 in vitro diagnostic devices are included on FDA's list of In Vitro Diagnostics EUAs . Laboratories should use an existing authorized nucleic acid assay, and, if not authorized for use with pooling, evaluate and validate the performance of that assay for a pooling strategy according to FDA's guidance in its Molecular Diagnostic Template for Laboratories . If laboratories modify the authorized assay by incorporating alternative components, including extraction methods, PCR instruments, and software versions, for the purposes of a pooling strategy, the laboratories should also evaluate and validate the performance of the altered test system.

Reporting Pooled Surveillance Testing Results

Results of surveillance testing can be returned in aggregate to the requesting institution, such as a university or public health agency. Negative pooled surveillance test results should be reported as "presumptive negative" to the requesting institution. Positive and indeterminate pooled surveillance test results should not be reported to the requesting institution; they should be retested individually before being reported in aggregate.

Facilities, regardless of their CLIA status, should not officially report the results of surveillance testing, including surveillance testing that uses a pooling procedure, to the local, state, tribal, or territory health department as diagnostic or screening test results. If a local, state, tribal, or territory health department requests access to the results of surveillance testing for SARS-CoV-2 that uses a pooling procedure, the laboratory should state in the report to the health department that the data are pooled surveillance testing results that do not represent COVID-19 diagnostic or screening test results.

Only a facility with a CLIA certificate may officially report a patient-specific diagnostic or screening COVID-19 test result to the local, state, tribal, or territory health department.

Facilities that conduct surveillance testing, including surveillance testing that uses a pooling procedure, should not report test results to individuals whose specimens have been tested, or to the individual's health care provider, employer, etc. If at any time a facility intends to report a patient-specific test result, it must first obtain a CLIA certificate and meet all requirements to perform testing. For more information, see CMS's summary of the CLIA regulations .

Limitations of Pooled Surveillance Testing

Based on limited data, using a pooling testing procedure for SARS-CoV-2 has some limitations. In a pooling procedure, the laboratory cannot ensure the diagnostic integrity of an individual specimen because it is combined with other specimens before testing. Specimen integrity can be affected by the quality of swab specimen collection, which could result in some swabs having limited amounts of viral genetic material for detection. Inadequate individual specimens, including those with limited amounts of viral genetic material, might not be eliminated from the pooled specimen before testing. Even if each individual specimen in a pool is adequate, the specimens in a pooled procedure are diluted, which could result in a low concentration of viral genetic material below the limit of

detection. These limitations mean that monitoring the prevalence of disease and properly validating the assay and the instrumentation are important to limit the potential for false-negative results. In general, the larger the pool of specimens, the higher the likelihood of generating false-negative results.

The prevalence of COVID-19 in a population also affects the efficiency of pooled testing strategies. In general, lower prevalence may enable a laboratory to use a larger optimal pool size. As the prevalence of COVID-19 increases, the cost savings of a pooling strategy decreases because more pooled tests will return positive results and those specimens will need to be retested individually.

CDC continues to pursue research studies on pooling strategies for testing for SARS-CoV-2 and will update this guidance as needed.

Summary Tables

Pooled Testing for SARS-CoV-2

	Surveillance Testing	Screening Testing	Diagnostic Testing
CLIA-Certified Laboratory	Yes	Yes	Yes
Non-CLIA-Certified Laboratory	Yes	No	No
CLIA Requirements Apply to Pooled Testing Procedure	No	Yes	Yes
Test System Must Be FDA Authorized	No	Yes	Yes

Reporting of Pooled SARS-CoV-2 Testing Results to State/Tribal/Local/Territorial (STLT) Health Departments

	Surveillance Testing	Screening Testing	Diagnostic Testing
Negative (-)	Return pooled results in aggregate to requesting institution (e.g., a university) as presumptive negative. Do not report to STLT health department as a diagnostic or screening result.	Report each individual in pool as negative to the STLT health department.	Report each individual in pool as negative to the STLT health department.*
Positive (+) or Indeterminate (+/-)**	Do not report pooled result. Perform individual testing and report individual results (+/-) in aggregate to requesting institution (e.g., a university). Do not report to STLT health department as a diagnostic or screening result.	Do not report pooled result. Perform diagnostic testing of individual specimens, and report each as (+) or (-) to the STLT health department.	Do not report pooled result. Perform diagnostic testing of individual specimens, and report each as (+) or (-) to the STLT health department.

*If the pool is subsequently tested individually, the pooled results should not be reported to the STLT health department; in that case, only the individual results should be reported.

**Positive/inconclusive pooled results should never be returned to STLT health department as a COVID-19 diagnostic or screening test result.

NOTE: For DoD labs with a Clinical Laboratory Improvement Program (CLIP) certificate, the term CLIA applies.

Returning of Pooled SARS-CoV-2 Testing Results to the Individuals in the Pool

	Surveillance Testing	Screening Testing	Diagnostic Testing
Negative (-)	Do not report to individuals in the pool.	Report to individual, individual's healthcare provider, employer, etc. according to the FDA-authorized assay's instructions for use.*	Report to individual, individual's healthcare provider, employer, etc. according to the FDA-authorized assay's instructions for use.*
Positive (+)	Do not report to individuals in the pool.	Do not report positive pooled results. Perform diagnostic testing of individual specimens, and then report to individual, individual's healthcare provider, employer, etc. as (+) or (-).	Do not report positive pooled results. Perform diagnostic testing of individual specimens, and then report to individual, individual's healthcare provider, employer, etc. as (+) or (-).
Indeterminate (+/-)	Do not report to individuals in the pool.	Do not report indeterminate pooled results. Perform diagnostic testing of individual specimens, and then report to individual, individual's healthcare provider, employer, etc. as (+) or (-).	Do not report indeterminate pooled results. Perform diagnostic testing of individual specimens, and then report to individual, individual's healthcare provider, employer, etc. as (+) or (-).

* The report given to the individuals in the pool should indicate that the testing procedure involved specimen pooling and explain the limitations of that type of testing.

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