

FACT SHEET FOR HEALTHCARE PROVIDERS

Twist Bioscience Corporation
SARS-CoV-2 NGS Assay

Updated: July 28, 2022

Coronavirus
Disease 2019
(COVID-19)

This Fact Sheet informs you of the significant known and potential risks and benefits of the emergency use of the Twist Bioscience Corporation's SARS-CoV-2 NGS Assay.

The SARS-CoV-2 NGS Assay is authorized for the qualitative detection of SARS-CoV-2 RNA in specimens (listed below) collected from individuals suspected of COVID-19 by their healthcare provider, and for the identification and differentiation of SARS-CoV-2 Phylogenetic Assignment of Named Global Outbreak

All patients whose specimens are tested with this assay will receive the Fact Sheet for Patients: Twist Bioscience SARS-CoV-2 NGS Assay.

(PANGO) lineages and specific SARS-CoV-2 genomic mutations from samples found to be positive using the SARS-CoV-2 NGS Assay when clinically indicated.

What are the symptoms of COVID-19?

Many patients with COVID-19 have developed fever and/or symptoms of acute respiratory illness (e.g., cough, dyspnea), although some individuals experience only mild symptoms, atypical symptoms, or no symptoms at all. The current information available to characterize the spectrum of clinical illness associated with COVID-19 suggests that, when present, symptoms include cough, shortness of breath or dyspnea, fever, chills, myalgias, headache, sore throat, new loss of taste or smell, nausea or vomiting or diarrhea. Signs and symptoms may appear any time from 2 to 14 days after exposure to the virus, and the median time to symptom onset is approximately 3-5 days. For further information on the symptoms of COVID-19 please see the link provided in "Where can I go for updates and more information?" section.

Public health officials have identified cases of COVID-19 throughout the world, including the United States. Please check the CDC COVID-19 webpage (see link provided in "Where can I go for updates and more information?" section at the end of this document) or your local jurisdiction's website for the most up to date information.

This test is to be performed only using respiratory specimens (listed below) collected from individuals suspected of having COVID-19. This test is also authorized for the identification and differentiation of SARS-CoV-2 PANGO lineages and specific viral mutations, when clinically indicated, from SARS-CoV-2-positive samples identified using the Twist Bioscience SARS-CoV-2 NGS Assay.

What do I need to know about COVID-19 testing?

Current information on COVID-19 for healthcare providers is available at CDC's webpage, *Information for Healthcare Professionals* (see links provided in "Where can I go for updates and more information?" section).

- The SARS-CoV-2 NGS Assay is a next generation sequencing (NGS) test on the Illumina NextSeq 500, 550, and 550Dx sequencing system intended for the qualitative detection of SARS-CoV-2 RNA in specimens collected from individuals suspected of COVID-19 by their healthcare provider, and for the identification and differentiation of specific SARS-CoV-2 genomic mutations and SARS-CoV-2 Phylogenetic Assignment of Named Global Outbreak (PANGO) lineages, when clinically indicated.
- The SARS-CoV-2 NGS Assay can be used to test nasopharyngeal (NP) swabs, oropharyngeal (OP) swabs, anterior nasal swabs, mid-turbinate nasal swabs, nasopharyngeal wash/aspirates, nasal wash/aspirate and bronchoalveolar lavage (BAL) specimens.
- The SARS-CoV-2 NGS Assay is intended to be used in conjunction with patient history and other diagnostic information, when clinically indicated, i.e., in situations where results may aid in determining appropriate clinical management.
- The SARS-CoV-2 NGS Assay is authorized for use in laboratories that are certified under Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, and meet requirements to perform high complexity tests.

Report Adverse events, including problems with test performance or results, to MedWatch by submitting the online FDA Form 3500 (<https://www.accessdata.fda.gov/scripts/medwatch/index.cfm?action=reporting.home>) or by calling 1-800-FDA-1088

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Specimens should be collected with appropriate infection control precautions. Current guidance is available at the CDC's website (see links provided in "*Where can I go for updates and more information?*" section).

When collecting and handling specimens from individuals suspected of being infected with the virus that causes COVID-19, appropriate personal protective equipment should be used as outlined in the CDC *Interim Laboratory Biosafety Guidelines for Handling and Processing Specimens Associated with Coronavirus Disease 2019 (COVID-19)*. For additional information, refer to CDC *Interim Guidelines for Collecting, Handling, and Testing Clinical Specimens from Persons Under Investigation (PUIs) for Coronavirus Disease 2019 (COVID-19)* (see links provided in "*Where can I go for updates and more information?*" section).

What does it mean if the specimen tests positive for SARS-CoV-2?

A positive test result for COVID-19 indicates that RNA from SARS-CoV-2 was detected, and therefore the patient is infected with the virus and presumed to be contagious. Laboratory test results should always be considered in the context of clinical observations and epidemiological data (such as local prevalence rates and current outbreak/epicenter locations) in making a final diagnosis and patient management decisions. Patient management should be made by a healthcare provider and follow current CDC guidelines.

The SARS-CoV-2 NGS Assay has been designed to minimize the likelihood of false positive test results. However, it is still possible that this test can give a false positive result, even when used in locations where the prevalence is below 5%. In the event of a false positive result, risks to patients could include the following: a recommendation for isolation of the patient, monitoring of household or other close contacts for symptoms, patient isolation that might limit contact with family or friends and may increase contact with other potentially COVID-19 patients, limits in the ability to work, delayed diagnosis of other conditions, and treatment for the true infection causing the symptoms, unnecessary prescription of a treatment or therapy, or other unintended adverse effects.

All laboratories using this test must follow the standard testing and reporting guidelines according to the appropriate public health authorities.

What does it mean if the test result is a SARS-CoV-2 lineage call and mutations report?

This test reports the viral mutations detected most reliably, and the lineage which is the best match for the virus in the sample. It is possible for a sample to contain additional mutations that are not reported if they are present only rarely, or if the sequencing quality is poor for that particular locus. It is possible for a lineage to be identified even if some of its characteristic mutations are not detected. Very occasionally new lineages of SARS-CoV-2 will arise which will be added to the reference database, which is updated regularly; however, if the lineage is very rare or new it may not be in the database yet.

The clinical applicability of SARS-CoV-2 mutation and lineage identification is under investigation as the virus continues to evolve. The presence of individual mutations does not always directly predict viral phenotype or clinical characteristics of the illness. Viral lineage represents a group of closely related viruses with a common ancestor, while individual mutations may occur within that definition. Healthcare providers may use the SARS-CoV-2 mutation and lineage information provided by the SARS-CoV-2 NGS Assay together with other laboratory and clinical findings as well as evolving scientific information in determining appropriate clinical management for their patient. For further information on SARS-CoV-2 viral lineage refer to the CDC *SARS-CoV-2 Variant Classifications and Definitions*, and for guidance on clinical management of COVID-19 please refer to the NIH *Coronavirus Disease 2019 (COVID-19) Treatment Guidelines* (see links provided in "*Where can I go for updates and more information?*" section).

Laboratory test results should always be considered in the context of clinical observations and epidemiological data (such as local prevalence rates and current outbreak/epicenter locations) in making final patient management decisions. Patient management should be made by a healthcare provider and follow current CDC and/or NIH guidelines.

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The SARS-CoV-2 NGS Assay has been designed to minimize the likelihood of incorrectly identifying SARS-CoV-2 mutations and lineage. In the event of incorrect SARS-CoV-2 mutations and/or lineage identification, risks to patients could potentially include the following: unnecessary or otherwise inappropriate treatment, including any associated adverse effects, or conversely, missed opportunity to initiate time-sensitive treatment. Specific risks may be identified with future evolution of the virus and available therapies.

All laboratories using this test must follow the standard testing and reporting guidelines, as appropriate, according to their appropriate public health authorities.

What does it mean if the test result is “invalid” or if SARS-CoV-2 is detected but no lineage call or mutation report is generated?

An “invalid” test result means the test could not return a reliable result due to a problem with the sample or the performance of the test (failed internal quality controls). When SARS-CoV-2 is detected but no lineage or mutation information is reported, it means that the genomic sequencing of the SARS-CoV-2 positive specimen was unsuccessful or of inadequate quality, and therefore no more detailed SARS-CoV-2 information could be reported for that sample. There can be a number of reasons why genomic sequencing was unsuccessful from a SARS-CoV-2 positive specimen, including if the concentration of the virus was too low or the quality of the specimen was degraded. Very occasionally new lineages of SARS-CoV-2 will arise which will be added to the PANGO reference database, which is updated regularly; however, if the lineage is very rare or new it may not be in the database yet, or its details may be changing. If clinically indicated, the healthcare provider may want to consider collecting additional specimens from the patient.

Risks to a patient of invalid or no result from the SARS-CoV-2 NGS Assay include: delayed treatment, resulting in missed opportunity to initiate time-sensitive treatment, or other unintended adverse events. ***The clinical management of COVID-19 should be initiated once a diagnosis has been made based on available information, established guidance, and the clinician’s judgment; initiation of treatment should***

not be delayed solely to obtain results of a mutation- or lineage-calling test.

The performance of this test was established based on the evaluation of a limited number of clinical specimens. The clinical performance has not been established in all possible variants but is anticipated to be reflective of the prevalent variants in circulation at the time and location of the clinical evaluation. Performance at the time of testing may vary depending on the variants circulating, including newly emerging lineages of SARS-CoV-2 and their prevalence, which change over time.

What does it mean if the specimen tests negative for SARS-CoV-2?

A negative test result for this test means that SARS-CoV-2 RNA was not present in the specimen above the limit of detection. However, a negative result does not rule out COVID-19 and should not be used as the sole basis for treatment or patient management decisions. It is possible to test a person too early or too late during SARS-CoV-2 infection to make an accurate diagnosis via the SARS-CoV-2 NGS Assay.

When diagnostic testing is negative, the possibility of a false negative result should be considered in the context of a patient’s recent exposures and the presence of clinical signs and symptoms consistent with COVID-19. The possibility of a false negative result should especially be considered if the patient’s recent exposures or clinical presentation indicate that COVID-19 is likely, and diagnostic tests for other causes of illness (e.g., other respiratory illness) are negative.

If COVID-19 is still suspected based on exposure history together with other clinical findings, re-testing with an alternative method should be considered by healthcare providers in consultation with public health authorities. Additional testing may be helpful to ensure testing was not conducted too early.

Risks to a patient of a false negative test result include: delayed or lack of supportive treatment, lack of monitoring of infected individuals and their household or other close contacts for symptoms resulting in increased risk of spread of COVID-19 within the community, or other unintended adverse events.

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What is an EUA?

The United States FDA has made this test available under an emergency access mechanism called an Emergency Use Authorization (EUA). The EUA is supported by the Secretary of Health and Human Service's (HHS's) declaration that circumstances exist to justify the emergency use of in vitro diagnostics (IVDs) for the detection and/or diagnosis of the virus that causes COVID-19. An IVD made available under an EUA has not undergone the same type of review as an FDA-approved or cleared IVD. FDA may issue an EUA when certain criteria are met, which includes that there are no adequate, approved, available alternatives, and based on the totality of scientific evidence available, it is reasonable to believe that this IVD may be effective in diagnosing COVID-19. The EUA for this test is in effect for the duration of the COVID-19 declaration justifying emergency use of IVDs, unless the declaration is terminated or the EUA is revoked (after which the test may no longer be used).

What are the approved available alternatives?

Any tests that have received full marketing status (e.g., cleared, approved), as opposed to an EUA, by FDA can be found by searching the medical device databases here: <https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/medical-device-databases>. A cleared or approved test should be used instead of a test made available under an EUA, when appropriate and available. FDA has issued EUAs for other tests that can be found at: <https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization>.

Where can I go for updates and more information?

CDC webpages:

General: <https://www.cdc.gov/coronavirus/2019-ncov/index.html>

Symptoms:

<https://www.cdc.gov/coronavirus/2019-ncov/symptoms-testing/symptoms.html>

Healthcare Professionals:

<https://www.cdc.gov/coronavirus/2019-nCoV/hcp/index.html>

Information for Laboratories:

<https://www.cdc.gov/coronavirus/2019-nCoV/lab/index.html>

Laboratory Biosafety: <https://www.cdc.gov/coronavirus/2019-nCoV/lab/lab-biosafety-guidelines.html>

Isolation Precautions in Healthcare Settings:

<https://www.cdc.gov/infectioncontrol/guidelines/isolation/index.html>

Specimen Collection: <https://www.cdc.gov/coronavirus/2019-nCoV/lab/guidelines-clinical-specimens.html>

Infection Control: <https://www.cdc.gov/coronavirus/2019-ncov/php/infection-control.html>

FDA webpages:

General: www.fda.gov/novelcoronavirus

EUAs: (includes links to fact sheet for individuals and manufacturer's instructions) <https://www.fda.gov/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/in-vitro-diagnostics-euas>

NIH webpages:

General: <https://www.covid19treatmentguidelines.nih.gov/>

Therapies: (includes information on antivirals and monoclonal antibody products)

<https://www.covid19treatmentguidelines.nih.gov/therapies/>

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